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ACTA RADIOLOGICA
EDITA IUSSU SOCIETATUM RADIOLOGICARUM
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VOL. 43 JUNE 1955 FASC. 6

SOME ASPECTS OF THE TECHNIQUE IN PELVIC PHLEBOGRAPHY

by

T. Greitz

The first report on phlebography of the pelvis seems to have been published in this journal in 1935 by HUTTER, who injected Perabrodil 40 % in the long saphenous vein or into the veins of the scrotum or penis. Since then, many papers dealing with changes in the pelvic veins have appeared. Different techniques have been used but as far as I have been able to ascertain, no discussion of the respective advantages of the different methods has been published.

Percutaneous injection into a superficial vein of the proximal part of the thigh or into a vein of the pubic region was used by BARKER and CAMP (1936), DOS SANTOS (1938), MARTORELL (1943), IMLER, BEAVER and SHEEHAN (1944), SERVELLE (1946), MOORE (1949), LINDBOM (1951) and GREITZ (1951). IMLER, BEAVER and SHEEHAN showed, in one case, that compression of one superficial collateral vein caused other similar veins to be filled. RAYMOND, ADAMS and MCCORRISTON (1948) selected the long saphenous vein proximal to the knee-joint for the injection. STOWERS and GROSSMAN (1946), FARIÑAS (1947), MOORE (1949) exposed the long saphenous vein. DOUGHERTY and HOMANS (1940), LESSER and DANELIUS (1944), LEGER and FRILEUX (1949) cut down upon the terminal branch of the short saphenous vein. Direct puncture of the femoral vein was used by O'LOUGHLIN (1947), BÄTZNER (1951) and OLIVIER (1951). A catheter method was employed by STARKLOFF, BRICKER, MC DONALD and LITZOW (1950), who exposed the long saphenous vein, and by ÖDMAN (1952), who inserted a polyethylene tube percutaneously in either the femoral or popliteal vein.

The intraosseous injection method of DRASNAR (1946) has been used by many authors. The popliteal femoral and iliac veins may be filled after an injection into the femoral condyles as shown by BEGG (1954).

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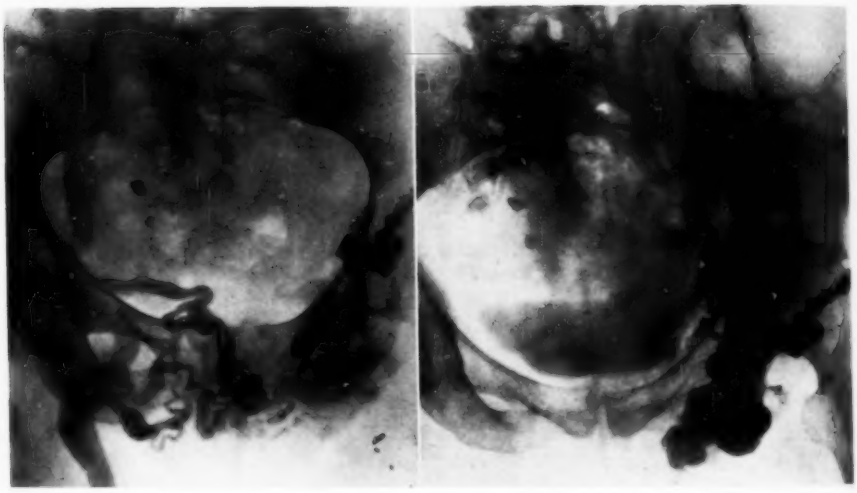
From Roentgen Department II (Director: Docent W. Magnusson), Södersjukhuset, Stockholm, Sweden.

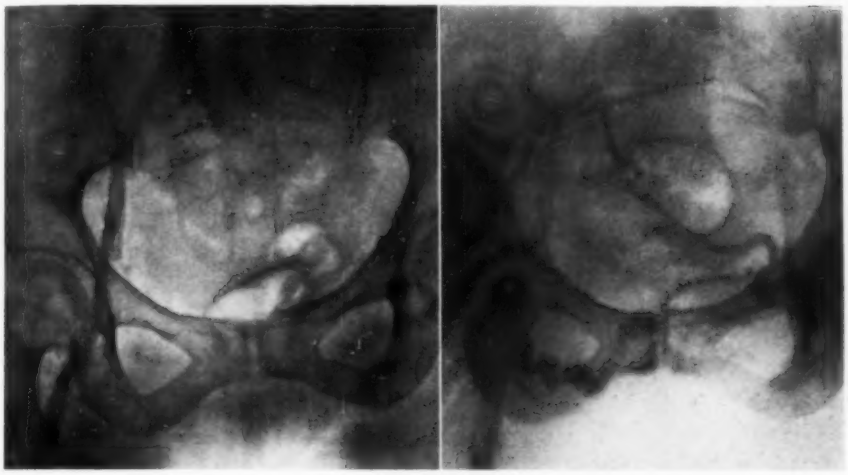


a b

Fig. 1. a. Injection into a vein in the left pubic region. The contrast medium passes only through the pubic varices to the right iliac vein, thus indicating total obstruction on the left side. b. Same case; same injection site. Compression applied to the pubic collaterals forcing the contrast medium into the left iliac vein, which is thus shown to be patent.

In recent years much interest in pelvic phlebography has been aroused, especially in France, by the work of DUCUING and co-operators. They chose five different sites for the injection, the pecten ossis pubis, the tuber ossis ischii, the crista iliaca, the sacrum and the trochanter major. This technique was devised primarily to demonstrate the internal iliac veins and their tributaries. For the same purpose, contrast medium was injected into a vein of the penis or the scrotum by HUTTER (1935), ROCCO and ROMUSSI (1949), BAUX and POULHES (1950) and DE LA PENA (1951).

In cases of chronic venous insufficiency, the external iliac vein should, however, be examined. I have, therefore, explored this vein by means of an additional pelvic phlebography in all cases in which the vein did not fill in the routine examination of the lower extremity. This was the case in 73 out of 310 phlebographies, in which different techniques were tried and an attempt was made to estimate their relative value. Practically all these examinations were performed with 30 ml Umbradil 35 % injected as rapidly as possible. Umbradil 50 % was employed in a few early cases but, in two of these, thrombophlebitis developed and the use of this concentration was discontinued.



a b

Fig. 2. a. Patient supine. The iliac vein is filled, contrast medium having been injected into a superficial vein in the distal part of the thigh. b. Same patient examined in the prone position; same injection site. Pubic collaterals, not filled in the preceding film, are now seen. Both iliac veins are incompletely filled.

1. *Injection into a superficial vein in the proximal part of the thigh or into pubic varices.* This technique was exclusively used at first. In phlebographies of the pelvis, films indicating a total occlusion of the ipsilateral iliac vein were obtained in 10 out of 14 cases. Compression of the pubic collaterals was, however, applied in three cases and patency demonstrated (Fig. 1). The results after injection into a superficial vein situated proximally were thus considered unreliable, especially as it was sometimes difficult to compress the collaterals without at the same time compressing the veins to be examined. This technique was, therefore, discontinued and in the 59 subsequent phlebographies of the pelvis no total block was found. In order to ascertain whether anything could be gained by placing the patient in the erect position, 3 cases were so examined; it was found that all or most of the contrast medium descended into the thigh.

2. *Injection into a superficial vein, either in the distal part of the thigh or at the level of the knee.* Even when the injection was performed in this region it was found impossible to carry out the supplementary phlebography of the pelvis with the patient erect; the contrast density, as shown in 3 cases, was very poor and no better than in the routine examination with injection carried out in to the dorsum of the foot.

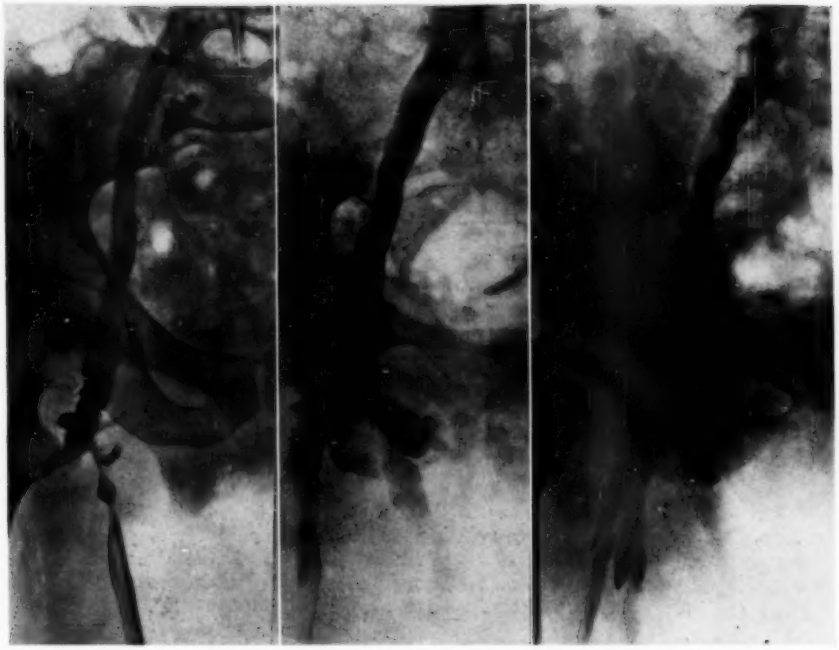


Fig. 3 4 a 4 b

Fig. 3. Catheter inserted via the long saphenous vein.

Fig. 4. Insertion of the polyethylene tube via the popliteal vein. a. prone. b. erect. Same findings.

A much better contrast filling of the iliac vein was, in these cases, obtained in the horizontal position. The studies were, therefore, continued with the patient recumbent. The supine and prone positions were compared in 15 cases by the examination of the same patient twice. The iliac vein or the collaterals around this vein — the peri-iliac veins — were better filled in the prone position in 9 cases; in one case, the filling was more satisfactory in the supine position; and in the remaining 5 cases, there was no appreciable difference. These findings allow no definite conclusions but if indeed there should be a generally better filling in the prone position, this may be due to the incline of the iliac vein, forcing the contrast medium to run 'uphill' in this position. There seem, however, to be certain advantages of examining the case in both positions, in as much as anatomic conditions, not seen in one position, may be demonstrated in the other (Fig. 2).

3. *Direct puncture of the femoral vein.* As the contrast filling of the deep main trunks after injection of a superficial vein is often unsatis-

a b

Fig. 5. Percutaneous insertion of a catheter into the femoral vein. a. Supine. Tortuous peri-iliac veins filled. b. Erect. Some varices in the upper part of the thigh are filled and the inferior vena cava is more clearly seen; otherwise no appreciable difference.

factory and thus gives a false idea of the true anatomy, the contrast medium was injected into the femoral vein. This technique gave a better filling of the deep veins but was used only in three cases as it was found difficult to change the position of the patient without displacing the needle. Since comparative examinations in different positions were desired, a catheter method was considered more suitable.

4. *The catheter method.* A catheter was introduced following percutaneous puncture in 20 cases, in 8 cases via the great saphenous vein, in 8 cases via the femoral, and in 4 cases via the popliteal vein (Figs. 3, 4, and 5). In another 16 cases, the insertion of the catheter was unsuccessful; this is a high percentage (about 45 %) of failures. These cases, however, represent a selection, as only those in which no filling of the pelvic veins was obtained in the routine phlebography with the patient erect, were examined. Obvious changes of the post-thrombotic type were found in 13 cases of these 16 failures. The catheter method cannot, therefore, be used exclusively.

In cases with poor filling of the iliac vein in the routine phlebography, the upper part of the femoral vein is also often unsatisfactorily filled. It may, however, be examined if the catheter is introduced via the popliteal vein, a more preferable procedure than its insertion via the femoral or saphenous veins.

Very good filling of the pelvic veins was obtained by means of a catheter in all cases, and far better than from an injection of a superficial vein. In 15 cases, double examinations (d. exams) were performed with the patient in both the recumbent and erect positions (65°). No considerable differences were observed, the filling being slightly better in the vertical position in 7 cases, whereas it was more satisfactory in the recumbent position in 2 cases; in 8 cases no difference could be discerned. With the patient erect, a retrograde flow of contrast medium in a few instances filled veins not visible in the recumbent position (Figs. 4 and 5). The filling was almost the same in the supine and prone positions whether the table was horizontal (4 d. exams) or tilted to 65° with the feet down (4 d. exams).

5. *Intraosseous injection.* The external iliac vein is filled after a contrast medium is injected into the trochanter major. This technique was used only in two cases. It seemed to produce poorer filling than the catheter method (1 d. exam). In one of these cases, a painful peritendinitis developed at the place of injection. In a third case, it was not possible to perforate the corticalis with the trocar designed for the purpose. (Injection into the femoral condyles as described by Begg was not used.)

Conclusions

In about 80 % of patients with chronic venous insufficiency, it is possible to fill the external iliac vein in routine phlebography in the erect position. In the remainder, a supplementary examination has to be made, the technique of which can never be quite uniform but must be varied from case to case. When the injection is made into a vein, the following principles seem to apply:

1. Injection into a superficial vein in the proximal part of the thigh or into pubic varices should not be employed, as this technique may give a false indication of a venous block on the ipsilateral side.

2. The catheter method should be used if possible. After the catheter is introduced, the patient is examined prone or supine and, if considered appropriate, in the erect position as well.

3. Insertion of the catheter into the popliteal vein is preferable.

4. If the puncture of the popliteal vein is unsuccessful or, due to changes seen in the preceding phlebograms, is considered impossible, the catheter is introduced into the long saphenous vein.

5. If the long saphenous vein is absent, not palpable, or otherwise not suitable for the insertion of a catheter, the femoral vein is punctured.

6. If the introduction of a catheter is considered impossible or has failed, a superficial vein distally in the thigh or at the level of the knee-joint is chosen for the injection; the patient is examined both in the prone and supine positions.

SUMMARY

Intravenous phlebography of the pelvis is discussed with special reference to its employment as a supplement to the routine examination of the leg in chronic venous insufficiency. Various methods have been tried and a comparative study is made.

ZUSAMMENFASSUNG

Die intravenöse Phlebographie des Bäckens wird unter besonderer Berücksichtigung ihrer Anwendung als ein Supplement zur Routineuntersuchung der Beine bei chronischer venöser Insuffizienz besprochen. Verschiedene Methoden sind versucht worden und eine vergleichende Studie hierüber wird angestellt.

RÉSUMÉ

L'auteur étudie la phlébographie pelvienne intraveineuse et s'attache particulièrement à son utilisation comme complément de l'examen habituel du membre inférieur dans l'insuffisance veineuse chronique. Il a essayé différentes méthodes et en fait une étude comparative.

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AORTIC STENOSIS ASSOCIATED WITH ANEURYSMAL DILATATION OF THE ASCENDING AORTA

by

Lucio Di Guglielmo and *Mariano Guttadauro*

During the last few years attention has been paid to certain cases of an unusual dilatation of the ascending aorta, described as a general increase in the calibre of the vessel to as much as four times its ordinary size. The deformity has almost always been limited to the ascending aorta and the proximal part of the arch and has never extended beyond the origin of the left subclavian artery at which point the vessel has returned more or less abruptly to its normal shape.

In 1918, BRONSON and SUTHERLAND reported the case of a child aged 6 with arachnodactylia, death occurring from a ruptured aneurysm of the ascending aorta "which was as large as the heart"; WEILL (1932) described the case of a woman, aged 27, suffering from arachnodactylia, "with well marked dilatation of the ascending aorta especially posteriorly and to the right". BAER et coll. (1943) were, however, the first to carry out a study from a clinical and anatomic point of view. They described two cases of arachnodactylia and aortic dilatation. One, a boy, aged 14, had on clinical examination "a loud systolic murmur with thrill" which reached its maximum at the sternum. The murmur could be heard also along the vessels of the neck; there was, in addition, a slight diastolic murmur at the base of the heart. These signs had been observed since birth. The post-mortem examination revealed hypertrophy of the left ventricle and a dilatation of the ascending aorta which had a maximum circumference of 14 cm. This conspicuous dilatation ceased abruptly shortly beyond the origin of the innominate artery. The aortic valves were normal. The second case was a man, 26 years of age, who had systolic and diastolic murmurs at the base of the heart. The post-mortem examination revealed marked hypertrophy of the left ventricle and "a transverse ridge in the endocardium below the aortic valve". Immediately

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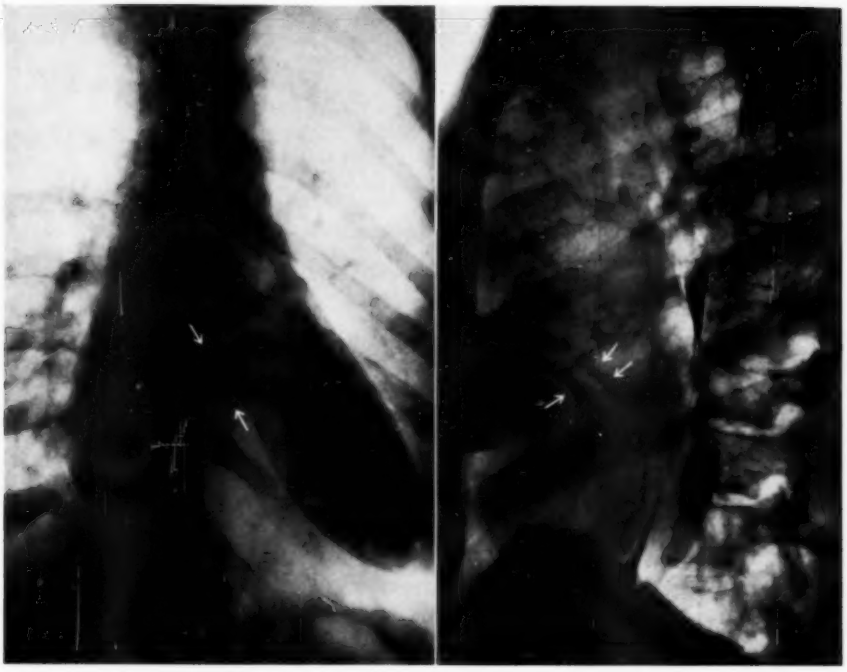


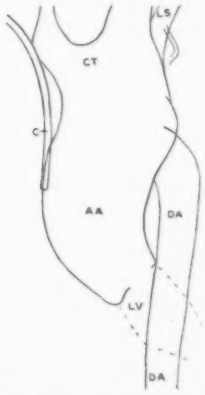
a b

Fig. 1. a. A.p. roentgenogram. b. Lateral projection. Calcifications at the site of the aortic valves.

above the aortic valves there was a dilatation of the ascending aorta with a maximum circumference of 19 cm.

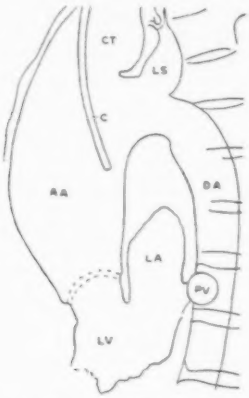
Histologic examination of sections taken from the aortas of both cases gave identical results: there were structural changes in the tunica media consisting in necrosis of the elastic tissue and collagen, with mucoid cyst formation, as in Erdheim's medionecrosis. These histologic features led the authors to the hypothesis that the dilatation of the vessel was due to malformation of the tunica media. In both instances, dilatation of the aorta had not been detected either by fluoroscopy or radiography.

Others later also published cases, 14 in all, of marked aortic dilatation (PARKER et coll., TOBIN et coll., LUTMAN et coll., REYNOLDS, TOURNIAIRE et coll., PROVENZALE, PETCH, SCHORR et coll., GRISHMAN et coll., LEWES, TRICOMI). Clinically there were signs of aortic valvular disease in all the 14 cases — except in that of TOURNIAIRE and his co-



2 a.

a. A.p. projection. AA = ascending aorta; DA = descending aorta; C = catheter in the superior vena cava; CT = common trunk and left carotid artery; LS = left subclavian artery; LV = left ventricle.



2 b.

b. Lateral projection. AA = ascending aorta; DA = descending aorta; C = catheter; CT = common trunk and left carotid artery; LA = left atrium; LV = left ventricle; LS = left subclavian artery; PV = pulmonary vein.

Fig. 2. Angiocardiography of the same case.

workers — and in some of them it was confirmed at post-mortem examination. In most instances (10 cases) the deformity of the aorta was associated with arachnodactylia. In 6 cases the histologic findings consisted in structural changes in the tunica media of the aorta. In the case described by TOURNIAIRE and his co-workers the structure of the aortic wall had, however, a normal appearance. There were no anatomic changes to indicate either aortic stenosis or incompetence.

Case report

Female, aged 32 years. No history of rheumatic fever. Slight dyspnea and palpitations from childhood with sensation of heat in the upper part of the trunk and swelling of the ankles. These symptoms became more and more pronounced in the course of time. Palpitations occurred even during rest together with thoracic pain, pricking in the fingers accompanied by flushing of the skin of the head. There was no cyanosis.

Physical examination: Skin pale. No cyanosis or dyspnea. No arachnodactylia. *Heart:* Thrill over the whole heart area reaching its maximum at the base; beat regular; loud systolic murmur at apex. There was a loud systolic murmur at the base as well as a diastolic rumble which reached its maximum in the 2nd right intercostal space. A systolic murmur was also heard in the interscapular region, very strong to the right, and also evident in the carotid and cubital arteries. *Arterial pressure:* Both arms, 110/90; both legs, 135/95. *ECG:* Right bundle branch block. Left ventricular strain. *Cardial function test* (NYLIN): Insufficiency for average work.

Roentgen examination: Heart volume 690 cc corresponding to 470 cc per sq. m of body surface. Thorax markedly flattened with the thoracic spine scoliotic. For this reason the shape of the heart and the great vessels were not properly shown. Deformity of the aorta (Fig. 1 a). Areas of calcification at the sides of the aortic valves (Figs. 1 b and 2 a).

Thoracic aortography could not be performed since it was impossible to introduce a catheter into the ascending aorta. *An angiocardiographic examination* was carried out. A No. 12 F catheter was introduced via a cubital vein to the superior vena cava. Sixty ml Umbradil 70 % were injected in two seconds. As soon as the opaque medium had passed the lung vessels, the left atrium, left ventricle and the aorta were clearly visualized (Fig. 2 b). The ascending aorta and aortic arch were considerably dilated. The dilatation began immediately beyond the aortic ostium and continued to a level one cm distal to the origin of the left subclavian artery. The sinuses of Valsalva were not visible. The ascending aorta at its maximum reached a diameter of 6 cm. The innominate and left carotid artery seemed to form one wide vessel which divided into its branches at the level of the jugulum. The proximal part of the left subclavian artery was also dilated, having a diameter of about 2 cm. There was no evidence of coarctation of the aorta.

Discussion

A diagnosis of aortic stenosis with marked post-stenotic dilatation of the aorta was made on the clinical and radiologic signs. The calcified areas in the aortic valves made it obvious that the stenosis was valvular (CONTRATTO and LEVINE, DAVIES and STEINER, DE FAZIO and MARSICO, PARKINSON). Besides the very harsh systolic murmur there was a diastolic

rumble at the base of the heart and ascending aorta. There were no other signs of aortic incompetence and probably the diastolic rumble was caused by diastolic reflux and whirlpools in the sac of the ascending aorta. TOURNIAIRE et coll. found a diastolic murmur in their case in which the valves were anatomically normal, and ascribed the murmur to whirls in the dilated aorta.

The aortic stenosis was in our case probably congenital, the first symptoms appearing in earliest childhood, while there was no history of rheumatic fever or any other disease which could have given rise to valvular endocarditis.

Congenital aortic stenosis was until a few years ago considered a rare disease (WALSH et coll.), but is now being diagnosed with increasing frequency (FRIEDBERG, GRISHMAN et coll.). There are two types. The lesion may be localized to the valves or immediately below the valves in the outflow tract. Clinically it is difficult to distinguish the two forms and, according to BROWN, there is no sign of subaortic stenosis which serves to differentiate it from stenosis of the valvular type. On the other hand, we believe that the latter may be diagnosed when there are calcified areas at the side of the aortic ostium. The angiocardiographic examination did not show any definite sign of stenosis. GRISHMAN et coll. have stressed the difficulty of showing aortic or subaortic stenosis. This is in contradistinction to the accuracy with which valvular or infundibular pulmonary stenosis can be demonstrated by means of selective angiocardiography (JÖNSSON et coll.). A similar method for distinct visualization of the left ventricle and aortic valves is lacking so far. In addition to the ascending aorta, the vessels issuing from the arch were markedly dilated. The sharp return of the aortic calibre to normal size beyond the left subclavian artery was very striking. This phenomenon has been described by many other authors and is quite in accordance with the hydromechanical laws which rule the appearance of poststenotic dilatation (HOLMAN).

In attempting an interpretation of the ectasia of the vessel we are confronted with two hypotheses. The malformative hypothesis, which is upheld by BAER and his colleagues and others, has its essential basis in histologic data deduced from the study of fragments from the dilated wall of the aorta. It is firmly supported by the observation that this kind of ectasia is often found in cases of arachnodactylia, a condition which in the modern literature is regarded as a mesenchymal dysplasia. The lesions which BAER observed, consisting of loss of density and breaking up of the elastic fibres in the tunica media with an increase in the chromotropic substance are due, according to COSTO-FLORENZ, to a persistence of a structural fetal state in the walls of the vessel. It should be noted, however, that alterations in the elastic texture of the media

do not always signify conditions of malformation. Changes in the elastic fibres with increase in the chromotropic substance ending in a final state of medionecrosis may also arise from an abnormal stream on the walls of the vessel caused by the vigorous haematic jet which results from a stenosis (ASCENZI).

In a very recent paper regarding 105 patients with Marfan's syndrome Mc KUSICK has emphasized the influence of the congenital weakness of the connective tissue on the genesis of the aortic abnormalities in this syndrome, *i. e.* dissecting aneurysm and diffuse aneurysm of the ascending aorta.

Other authors (MONTALDO, CAMPBELL and KAUNTZE) have laid stress on mechanical factors in explaining poststenotic dilatation. Experimental researches were carried out by CAVINA who induced stenosis of the pulmonary artery in young rabbits by tying a silk thread around the vessels, immediately adjacent to its point of origin. Aneurysmal dilatation in the trunk of the pulmonary artery, never extending beyond the bifurcation, was constantly observed.

In 1954, HOLMAN published a comprehensive study on this subject. After a review of the literature, and on the basis of interesting experiments, he argued in a convincing manner that poststenotic dilatation may be caused by purely hydromechanical factors. A mass of fluid ejected through a narrow and limited constriction under high velocity strikes against a more slowly moving mass of liquid distal to the stenosis. This results, first, in the conversion of high kinetic energy into potential energy or lateral pressure and, secondly, in the lateral deflection of the rapid stream and even in a complete reversal direction of flow. The two streams meet and produce eddies of alternating high and low pressures, the repeated impacts of which, over a prolonged period against an elastic wall, are capable of inducing its structural fatigue and distension (HOLMAN). In selective angiocardiography of valvular pulmonary stenosis, such eddies are always seen in the dilated pulmonary artery and this can be considered as a radiographic demonstration of the hydromechanical factors which cause poststenotic dilatation (JÖNSSON).

In the case we have described the presence of valvular calcifications indicates the existence of aortic stenosis and there was no arachnodactylia or other signs of mesenchymal dysplasia. The observations of CAVINA, HOLMES, ASCENZI and HOLMAN quoted demonstrate that all characteristics of poststenotic dilatation may be explained as results of mechanical factors. On the other hand, aortic congenital stenosis is not always associated with such a dilatation of the ascending aorta. Furthermore, in those patients in whom no valvular changes were demonstrated (BEAR et coll., TOURNIAIRE et coll.) the aortic dilatation may be explained only on the basis of a congenital dysplasia.

One must conclude that although in some cases the hydromechanical factors predominate in the genesis of this uncommon dilatation of the aorta, in others the dysplasia due to malformation may constitute the basis of the lesion.

SUMMARY

The clinical, roentgenologic and angiocardiographic findings are described in a case of congenital valvular aortic stenosis with dilatation of the ascending aorta and calcification of the valves. A brief summary of 14 cases from the literature is presented.

ZUSAMMENFASSUNG

Die klinischen, röntgenologischen und angiokardiographischen Befunde in einem Fall mit kongenitaler Aortaklappenstenose mit Erweiterung der Aorta ascendens und Verkalkung der Klappen werden beschrieben. Eine kurze Zusammenfassung von 14 Fällen aus der Literatur wird vorgelegt.

RÉSUMÉ

Description des signes cliniques, radiographiques et angiocardiographiques dans un cas de sténose aortique valvulaire congénitale, avec dilatation de l'aorte ascendante et calcification des valvules. Bref résumé de 14 cas de la littérature.

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ARTHROGRAPHY OF THE ELBOW-JOINT

by

H. Arvidsson and *O. Johansson*

During recent years the investigation of joints by means of a contrast medium has proved a valuable complement to the clinical examination. LINDBLOM, inter alios, has shown the usefulness of a contrast medium examination of the knee-joint for determining meniscus and cruciate ligament ruptures. The technique of knee arthrography with a positive contrast agent has improved so that it must now be considered a routine procedure; it has proved particularly successful in the examination of the shoulder and hip-joints. However, very few reports of contrast medium investigations of the elbow-joint are found, although LINDBLOM (1953) has briefly discussed the method and possibilities in a general survey of arthrographies.

In order to make clear the possibilities of arthrography of the elbow-joint with a positive contrast medium, we have examined fresh elbow injuries and some cases of chronic diseases of the elbow-joint, such as osteochondritis and epicondylitis. Some cases have been operated on, so that the arthrography findings have been directly compared to the actual extent of the injury.

Technique and anatomy

To puncture the elbow-joint is a relatively simple procedure. The puncture is preferably made proximal to the radial head — partly because it is possible to locate this site by means of palpation, even if there is a swelling after trauma, and partly because leakage of the contrast medium will not disturb the visualization of the medial part of the capsule, in which most of the ruptures are found.

The joint is punctured after local anaesthesia. A medium-sized needle (internal diameter 0.50 to 0.75 mm) should be used, since it is often impossible to suck out the admixed blood and viscous synovial fluid with a fine needle. The synovial fluid is expressed by means of gentle pressure over the joint. A 35 per cent iodopyracet solution (Umbradil) is in-

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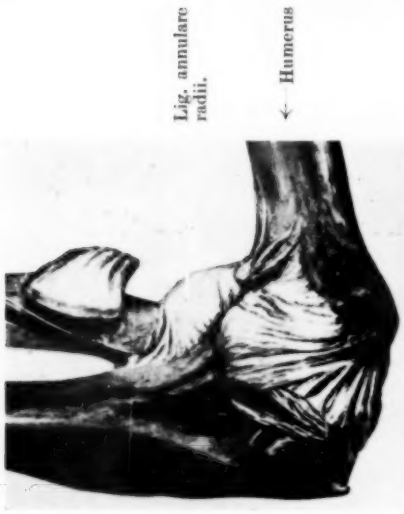


Fig. 1. Medial aspect of the elbow.

Fig. 2. Lateral aspect of the elbow.

jected slowly until the patient has a feeling of moderate tension in the elbow. As a rule, 5 to 6 ml has proved to be adequate, but if the capsule has been distended with blood it is necessary to inject up to 10 ml in order to obtain satisfactory contrast filling of the joint. In the beginning all patients were examined in the sitting position. In some cases, however, the patient complained of nausea immediately after the injection and, later, most of the examinations were performed with the patient recumbent. After the medium has been distributed throughout the joint by gentle movements, the following views are obtained:

1) lateral in 90° flexion, 2) lateral in extension, 3) A—P, 4) oblique for free projection of the medial capsule contour. When the activity of the patient has not been restricted by the injury, we recommended that the arm examined should be kept at rest for 24 hours. In a small number of our cases the patient felt uncomfortable after the examina-

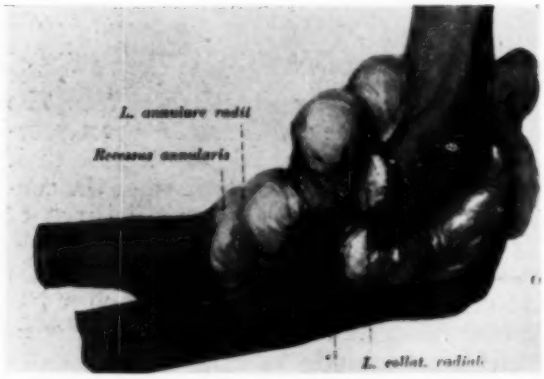


Fig. 3. Lateral aspect of a wax-injected elbow. Note the large anterior and posterior recesses.

a b

Fig. 4 a and b. ♂ 52 years. Normal case. *Arthrography:* Large anterior recess. Partial filling of the annular recess. Note the irregularity of the capsule border at the medial collateral ligament.

tion, although this was only in immediate connection with the injection of the contrast medium. No other complications were observed.

With regard to the normal anatomy of the elbow-joint the reader is referred to current handbooks of anatomy. There is an excellent survey on the subject in FICK: Handbuch der Gelenke. In that which follows, anatomic details of importance in the interpretation of the arthrogram will be briefly discussed. The medial and lateral ligaments of the elbow are shown in Figs. 1 and 2. These ligaments act as reinforcements to the capsular ligament, and are in fact closely attached to it. The lateral ligament is a triangular band, the apex of which is fixed to the lateral epicondyle of the humerus. Distally, the middle part of the base of the ligament blends with the annular ligament of the radius, and the thicker portions before and behind are attached to the margins of the radial notch. The medial ligament is composed of three bands, anterior, posterior and transverse, and stretches from the medial epicondyle of the

Fig. 5. ♀ 58 years. Fracture of the head of radius. *Arthrography:* No capsule rupture. Typical puncture leakage.

humerus to the proximal end of ulna. Fig. 3 shows the shape of the joint after wax injection.

The normal arthrogram (Fig. 4) demonstrates the boundaries of the joint cavity; ten normal elbows were investigated. It is possible to determine the thickness of the joint cartilage. The large anterior and smaller posterior capsular recesses are visible in the lateral view. The annular recess, which is situated distally to the annular ligament is partly contrast filled. Distally to the medial epicondyle, corresponding to the medial collateral ligament, the contour of the capsule is rugged. This phenomenon is common in normal cases and not of pathologic significance. There are considerable variations in the appearance of the recesses. As regards the form and filling of the annular recess, the variations seem to depend on the technical performance of the investigation.

Material

In all, 97 elbow-joints have been examined. In some cases the same patient has been examined on both sides.

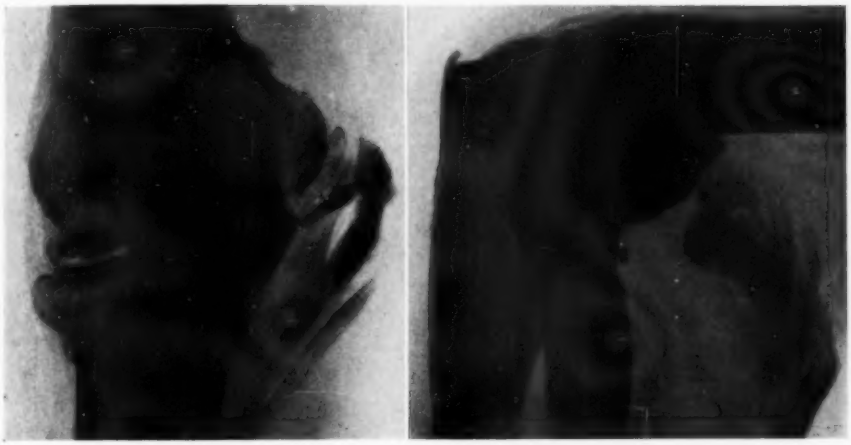
The cases characterized as pathologic have contrast medium outside the normal capsular boundaries. It must be emphasized that the time interval between injury and arthrography seems to be of significance. It is probable, especially in the case of small ruptures of the capsule that a leakage is difficult to demonstrate after a few days since fibrin clots coat the rupture.

The collocation of the material according to type of injury and sex is shown in Table I. Fractures of the head and neck of radius constituted the main part of the material. The ligament-capsule rupture in these cases occurred at the medial ligament (Fig. 6). Exceptions from this rule were some cases of comminuted fractures, in which there was sometimes rupture of the capsule near the head of the radius (Fig. 8). In the group of fractures of the head and neck of the radius, the greater number of the arthrographies were negative. The sex distribution seems to be noteworthy. In the male group, combination of injury of the head and neck of radius and of the medial ligament was more common than in

Table I

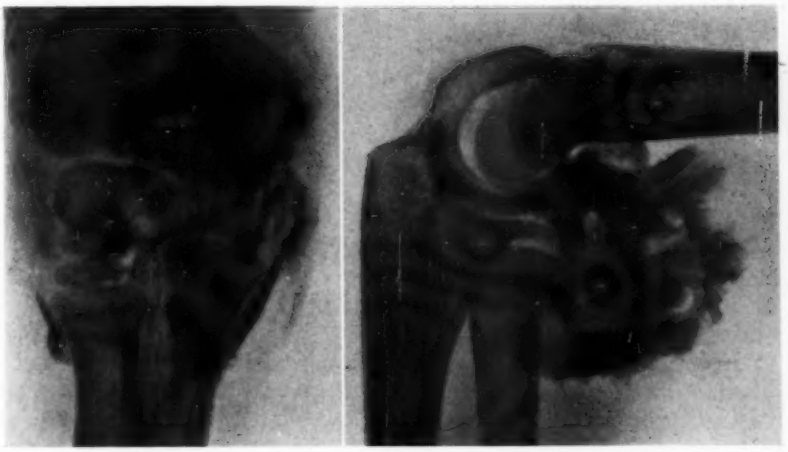
Arthrographies arranged according to type of injury and sex.

	normal		pathologic	
	♂	♀	♂	♀
1. Fractures of the head and neck of radius	5	22	12	5
2. Dislocations, posterior and lateral	—	—	5	8
3. Distorsions (no fracture)	9	6	4	2
4. Fractures of the elbow, other than 1	1	1	7	4
5. Osteochondritis, epicondylitis	3	3	—	—
	18	32	28	19



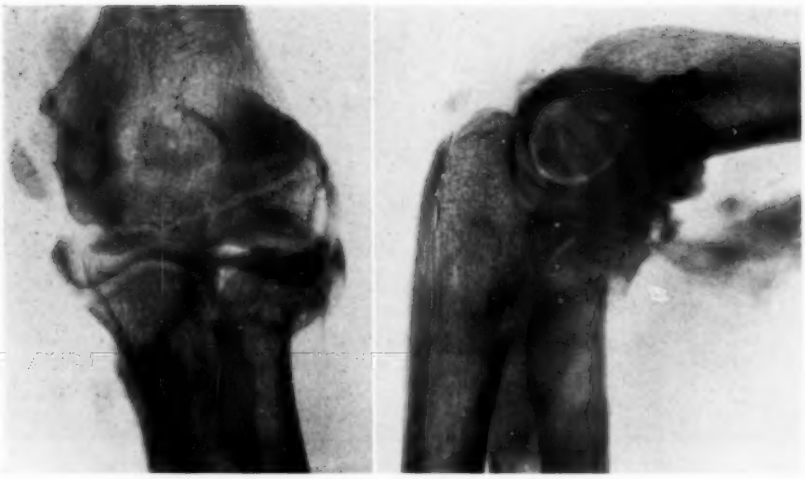
a b

Fig. 6 a and b. ♂ 58 years. *Arthrography* 6 days after injury: Small rupture at the medial ligament. Operatively verified.



a b

Fig. 7 a and b. ♂ 9 years. Posterior radial dislocation of radius and ulna. Dislocation of the medial epicondyle of humerus. *Arthrography* 3 days after injury, dislocation reduced: Large rupture in the medial-anterior part of the capsule.



a b

Fig. 8 a and b. ♂ 11 years. Subcapitular fracture of the radius with dislocation of the head. *Arthrography* 1 day after injury: Rupture of the medial ligament and the annular recess. Operatively verified.

the female group, although the material is too small for statistical conclusions. An explanation of this fact may be found in the different valgoid formation of the elbow-joint in males and females. The greater 'angulation' of the female elbow might increase the tendency to capitular compression, but on the other hand prevent the medial ligament from rupturing. In this respect there seems to be a similarity between the elbow- and knee-joint.

In all cases of dislocations of the elbow the position and extent of the ligament-capsule rupture was established. Clinically, there were two main types of dislocation.

1) Posterior dislocation of radius and ulna, which ensued from hyperextensive force.

2) Lateral dislocation, which arose from abduction force. The posterior dislocation was sometimes combined with a moderate degree of dislocation laterally or medially. In lateral dislocations, there was almost always a posterior dislocation as well but the former dominated the clinical picture of the injury. The boundary-line between the two types of dislocation is thus indistinct.

We have made an attempt to analyse the different types of capsular injuries that result from dislocations of the elbow. In lateral dislocations, the rupture usually occurred at the medial ligament. In posterior dislocations, there was a stretching of the anterior capsular recess with the inevitable rupture anteriorly.

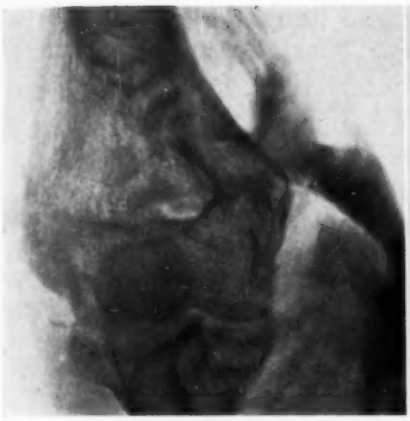


Fig. 9

Fig. 10

Figs. 9 and 10. ♀ 49 years. Radial-posterior dislocation of radius and ulna. Fracture of the head of radius. *Arthrography* 2 days after injury, dislocation reduced: Rupture of the medial ligament.

Fig. 11

Fig. 12

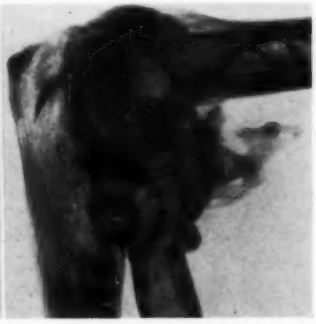


Fig. 13

Figs. 11, 12 and 13. Same case as in Figs. 9 and 10, seven months later. Myositis ossificans. Rupture healed. (Fig. 11 without contrast.)

Fractures of the coronoid process must be interpreted as tear fractures (PALMER) and are therefore a type of ligament injury. In the presence of such a fracture one must always suspect dislocation violence, either of the abduction or hyperextension type. In children the radial dislocation was often combined with avulsion of the medial epicondylar epiphysis. This injury has the same genesis as the medial ligament tear in adults (Fig. 7).

Arthrography was, in some cases, made without any signs of fracture or dislocation. Injuries that could be expected to cause ligament rupture

were investigated; there were several cases with large ruptures of the capsule in this group. Finally, we examined a few cases of osteochondritis and epicondylitis. This group was small, mainly because we did not obtain positive information from the first investigations.

Discussion

As is clear from the above, arthrography of the elbow-joint is a relatively simple investigation. It has been performed in some hundred cases without any complications and has given information of soft tissue injuries of the joint. Arthrography ought to be a guide in judging the size and situation of ligament ruptures of the elbow; following it, a plan for the further investigation must be drawn up. Together with the clinical data, arthrography gives the indication for operation, the results of which, in these joint injuries, are good; the material will be reported from a general clinical point of view later on.

SUMMARY

The authors have, in some 100 cases of injuries and other pathologic conditions of the elbow-joint, carried out arthrography with a positive contrast medium. In several cases ruptures of the capsule and collateral ligament have been found. The situation of these ruptures has varied with the type of injury. Several cases have been operated on and the roentgenologic diagnosis has proved to be correct.

ZUSAMMENFASSUNG

Die Verfasser haben in etwa 100 Fällen mit traumatischen Schädigungen und anderen pathologischen Zuständen des Ellenbogengelenkes die Arthrographie mit einem positiven Kontrastmittel ausgeführt. In mehreren Fällen sind Rupturen der Kapsel und der kollateralen Ligamente gefunden worden. Die Stelle dieser Rupturen variierte mit dem Typ der Schädigung. Mehrere Fälle sind anschliessend operiert worden und die Röntgendiagnose wurde dabei bestätigt.

RÉSUMÉ

Les auteurs ont pratiqué, dans environ 100 cas de traumatismes et d'autres affections de l'articulation du coude, des arthrographies avec un produit de contraste positif. Ils ont trouvé dans plusieurs cas des ruptures de la capsule et des ligaments latéraux. Le siège de ces ruptures variait suivant le type du traumatisme. Plusieurs cas ont été opérés et le diagnostic radiologique s'est montré correct.

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COARCTATION OF THE AORTA IN UNUSUAL SITES

by

Bengt Hulting and *Aado Vendsalu*

Our knowledge of the clinical picture and pathologic anatomy of typical coarctation of the aorta is well established. A detailed anatomic representation of the stenosis and of the collateral system is obtained by means of thoracic aortography. In rare instances, coarctation may be revealed in the lower thoracic or the abdominal aorta.

Six cases of coarctation of the aorta with this particular location are reported in the literature as incidental autopsy findings (6, 8, 9, 11, 12, 13). This diagnosis was also arrived at in another five published cases by means of angiocardio- and aortography (1, 2, 4, 5, 7). In one case (10), angiocardiography was unsatisfactory; typical coarctation was believed to be present, but at operation a stenosis was found just above the diaphragm. Finally, in a case (4) examined by means of retrograde carotid arteriography, a diagnosis of typical coarctation could be excluded; coarctation of the aorta in an unusual situation was accordingly assumed to be present though the diagnosis was not verifiable.

During the period from 1947 to April 1953, 90 cases, 66 male and 24 female, of typical coarctation of the aorta, were diagnosed at Roentgen Department I in co-operation with Medical Clinic II of Södersjukhuset, Stockholm, as well as 2 cases, both female, of coarctation in unusual sites. In these two latter cases, one, described by JÖNSSON et coll. (7), revealed a stenosis, 3 cm in length, in the distal part of the thoracic aorta with an aneurysmal dilatation immediately below it. The other is the case described below.

A girl, aged 10, was found to have elevated blood pressure in the upper half of the body: 180/90 in the arms, and 120/80 in the legs. Her symptoms were palpitation on physical exertion, occasional pricking sensations over the cardiac region, and slight headache. She was admitted to hospital with a diagnosis of coarctation of the aorta. Phys. exam.: Good general condition. No signs of decompensation at rest. Distinctly in-

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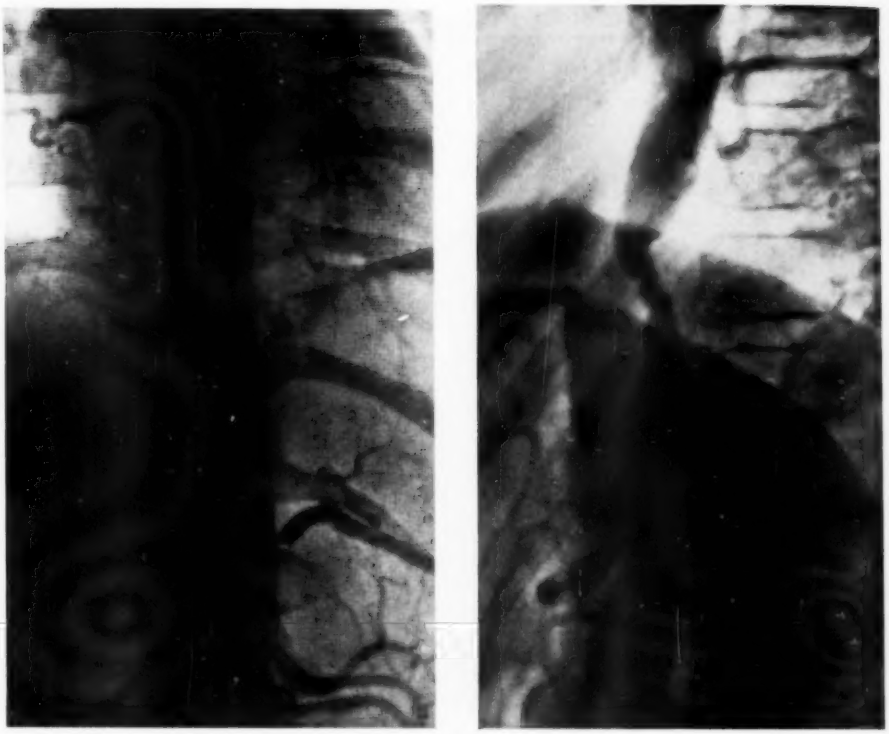

Fig. 1. Frontal (left) and lateral (right) view of the coarctation at the level of the diaphragm.

creased pulsations in the neck, the same on both sides. Faintly pulsating arteries in the thoracic wall (possibly collaterals). Soft systolic murmur of 2nd degree over the whole heart with the punctum maximum close to the left sternal edge in the third interspace. The second sound over the aortic area was slightly accentuated. A soft protracted and rhythmic murmur, decreasing in intensity in a caudal direction, was heard in the epigastrium. A murmur of a similar character, increasing caudally, with the punctum maximum at the level of the bases of the lungs, was present in the interscapular region. Blood pressure in the arms equalled 170/100, in the legs 115/90. Normal ECG. Oscillography: Pronouncedly decreased deflections in the legs at all levels. Blood pressure in the legs approx. 110 mm Hg; in the arms about 140 mm Hg.

Angiocardiography: 35 ml Umbradil 70 % were injected in barely two seconds through a catheter No. 9 into the pulmonary artery. The first films were exposed three seconds after the injection was initiated. The contrast medium passed mainly through the left lung, though its passage was evidently very slow, and the contrast medium in the left half of the heart and the aorta was poorly visualized; no details could therefore be discerned with any certainty. No constriction in the ascending aorta, the aortic arch,

or in the upper part of the descending aorta, evident. A constriction was suspected at the level of the diaphragm; it was uncertain owing to the small amount of contrast medium present.

Thoracic and abdominal aortography: With the tip of the catheter lying at the origin of the left subclavian artery, 40 ml Umbradil 50 % were injected in two seconds. Since no pathologic changes had previously been observed in the arch of the aorta or in the upper part of the descending aorta, only the lower part of the thoracic aorta and the abdominal aorta were examined on this occasion. A distinct constriction was now perceived in the lumen of the vessel at the level of the diaphragm. The diameter of the aorta above and below the constriction measured a good 1.5 cm in the roentgenograms, but at the maximum constriction, equalled only 4 mm. This marked constriction comprised a length of about 1.5 cm. Above and below, the lumen of the aorta widened conically for a distance of 2 cm. Around the stenosis, a number of collaterals, not particularly developed, were found (Fig. 1).

A narrowing of the lumen of the aorta at the level of the diaphragm was also observed on catheterization. The tip of the catheter could be passed through the stenosis and the pressure was measured above and below it.

ABBOTT (14) gives the ratio between men and women in typical coarctation of the aorta as 4 : 1. Of the cases reported of atypically situated coarctation, 2 were men and 10 women.

The published cases of coarctation of the aorta in unusual sites constitute a heterogeneous group as regards the etiology as well as the length and situation of the stenosis. In a few instances, the etiology could be ascertained by patho-anatomic examination. The stenosis of a length of one decimeter reported by GLENN et coll. (5) in a patient suffering from Recklinghausen's disease was caused by a neurofibroma which embraced the aorta in a cuff-like fashion. In a case published by BAHNSON et coll. (1), inflammatory changes around the aortic stenosis, with the lung adherent, were found at operation. HASLER (6) mentioned an organized thrombosis with a secondary shrivelling of the aorta as a probable cause in his case. Other authors have stated that the stenosis had a congenital origin. In some of these instances inflammatory, neoplastic, or degenerative changes, could be excluded by patho-anatomic examination. Two cases disclosed other congenital malformations (4, 8).

The situation of the stenosis varied from the lower part of the thoracic aorta to just distally of the renal arteries. The length of the stenosis was from 1 cm to 3 cm except in the cases described by GLENN et coll. (5) and BEATTIE et coll. (2) who noted a length of 10 cm and 6 cm, respectively.

The clinical findings in our case are identical with those observed in typical coarctation of the aorta. Accordingly, there seems to be no possibility of a differential diagnosis simply by means of those data. KONDO et coll. (8) attribute a differential diagnostic value to the periumbilical situation of the murmur. Furthermore, other authors state that they found the maximum intensity of the murmur in the epigastrium or

over the lumbar spine (1, 2, 4, 5, 9). This situation of the murmur occurred, however, in several of our cases of typical coarctation of the aorta.

Our case revealed no changes in the conventional roentgenograms, except that the left subclavian artery seemed widened. This suggestion of a deformity of the mediastinum was the only roentgenographic sign found to support the clinical suggestion of ordinary coarctation of the aorta. Notchings of the ribs were lacking. No dilated internal mammary arteries were observed in the lateral view (15).

In the 9 cases examined roentgenologically, and published earlier, no deformity of the mediastinum seems to have been present (1, 2, 4, 5, 7, 8, 9, 10). In 2 of these cases, rib notchings were described. The case reported by BEATTIE et coll. (2) had notchings only in the caudal ribs, being most conspicuous in the ninth and tenth ribs. FREEMAN et coll. (4), in their case, trace the situation of the changes to the lower ribs.

Deformity of the left mediastinal contour, as observed in practically all cases of typical coarctation of the aorta, seems either to be lacking or only insignificant in atypically situated coarctation. This may be attributed to the fact that in the latter the deformity is caused by a dilatation of the left subclavian artery only or by a less-marked development of the collateral circulation in the upper part of the thorax as a result of the caudal position of the stenosis. BRAMWELL and JONES (3) found the costal notchings in typical coarctation of the aorta to be localized to the third to eighth ribs. In the two cases described by BEATTIE et coll. (2) and FREEMAN et coll. (4) the notchings occurred only on the caudal ribs. This situation of the notchings should suggest atypically situated coarctation.

Angiocardiography, with the injection of contrast medium into the pulmonary artery, in our case proved that there was no narrowing of the ascending aorta, the aortic arch, or the upper part of the descending aorta. A constriction was suspected at the level of the diaphragm. The finding was regarded as uncertain, however, owing to the small amount of contrast medium present. Nevertheless, it was later verified by thoracic and abdominal aortography.

The present case serves to emphasize the necessity of repeating the examination with exposure of the whole thoracic and abdominal aorta before atypically situated coarctation can be excluded in cases with a clinical suggestion of coarctation of the aorta but with negative findings on angiocardio- or aortography.

The cases published in the literature seem to demonstrate that the prognosis is the same as in typical coarctation of the aorta. In a few instances, complications set in early (6, 7, 8). It is therefore essential that cases of atypically situated coarctation are also submitted to sur-

gery. These cases were earlier considered to be inoperable, but the development of surgical technique, particularly as regards grafting, has in the past few years rendered such intervention possible. The case published by BEATTIE et coll. (2) was successfully operated upon and grafting performed in 1951. In the case described by GLENN et coll. (5) in 1952, splenectomy and an anastomosis between the splenic artery and the thoracic aorta, proximally to the stenosis, were carried out.

SUMMARY

A case of coarctation of the aorta at the level of the diaphragm is described. With a survey of cases published earlier, the differential diagnosis with typical coarctation of the aorta is discussed.

The roentgenologic examination will suggest atypically coarctation when the deformity of the left mediastinal contour is absent or inconspicuous, or the costal notchings are localized to only the caudal ribs.

ZUSAMMENFASSUNG

Ein Fall einer Coarctatio aortae in der Höhe des Diaphragmas wird beschrieben. Im Zusammenhang mit einer Übersicht über früher veröffentlichte Fälle wird die Differentialdiagnose gegenüber der typischen Coarctatio aortae besprochen.

Die röntgenologische Untersuchung deutet auf eine atypische Coarctatio hin, wenn die Deformität des linken Mediastinalumrisses fehlt oder nahezu unmerkbar ist, oder die Rippenincisuren ausschliesslich in den kaudalen Rippen gelegen sind.

RÉSUMÉ

Description d'un cas de coarctation de l'aorte au niveau du diaphragme. Les auteurs passent en revue les cas déjà publiés et discutent le diagnostic différentiel avec la coarctation typique de l'aorte.

L'examen radiologique fera penser à une coarctation atypique quand la déformation du contour médiastinal gauche est absente ou infime, ou quand les encoches costales sont localisées aux seules côtes inférieures.

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A MICROANGIOGRAPHIC STUDY ON THE EFFECT OF GONADOTROPHIN UPON THE BLOOD VESSEL SYSTEM OF THE OVARIES OF RABBITS

by

Sven Bellman and *Bengt Engfeldt.*

The anatomy and function of the blood vessels of the ovaries have been studied in experimental animals and human material by several authors using various methods. In most of the work the blood vessels were filled with dyes or visualized by blood cell staining, and studied histologically in cleared sections. BASSETT (1943), employing such methods, made a thorough study of the ovarian blood vessels in albino rats.

The injection of neoprene or similar substances and subsequent maceration has proved valuable in other work dealing with blood vessel anatomy and was adopted by REYNOLDS and co-workers. In a series of papers (1947—1950) they reported studies on the spiral arteries both in human ovaries and those of experimental animals, and demonstrated typical age variations in the shape of the vessels. They also showed in rabbits that the spiral arteries became more extended following the administration of gonadotrophin and believed that the decreased spiralization influenced the blood supply to the ovaries and consequently also the supply of specific regulatory hormones to these organs. DELSON et coll. (1948) produced cysts in the ovaries of experimental animals by prolonged administration of gonadotrophin and concluded that these were caused by decreased spiralization of the ovarian arteries.

Histologic methods permit detailed studies on the smallest blood vessels. The small focal depth of the light microscope, however, makes it impossible to obtain well-defined simultaneous images of the small vessels in large tissue volumes. Neoprene casts of the vessels permit studies of large tissue volumes, but the filling in the smallest vessels is

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often fragmentary. Moreover, no comparison can be made between the histologic structure of the tissue and its blood vessel pattern.

Radiographic methods were first utilized in the study of ovarian blood vessels by BELOU (1934) who, in his atlas of the human blood vessel system, demonstrated the large blood vessels of the ovaries in unmagnified stereoradiograms. Later BELLMAN et coll. (1953) applied stereomicroradiography to the investigation of the transformation of the blood supply of follicles and corpora lutea during the oestrus cycle in albino rats.

All previous work described here was made on sacrificed animals or on surgical or autopsy material.

In the present work we have studied the reactions which arise in the blood vessel system of rabbit ovaries after the administration of gonadotrophin. Experiments, using vital microscopy and a modified microangiographic method, have been made both in sacrificed animals according to the technique described by BELLMAN (1953), and in living animals. The latter method has enabled us to compare the vascular pattern in the same ovary before and after the administration of the hormone.

Material and methods

Thirty-two mature female rabbits weighing 2 to 3.5 kg were used for the experiments. The animals were anaesthetized with Nembutal (20 mg/kg body weight) intravenously, and with ether. The abdomen was opened and the left ovary, which was most readily accessible, was placed on a metal plate by which it was supported during the inspection and the exposure of the microangiograms. The ovary and the opened abdomen were irrigated with warm physiologic saline during the experiments.

The vital microscopy was performed with a Zeiss Opton dissecting microscope at a magnification $\times$ 10.

The microangiograms in living animals were obtained with a Machlett OEG 50 roentgen tube with a tungsten target and a 0.2 mm thick beryllium window. The tube was run at 43 kV full-wave rectified pulsating d. c. and 11 mA. The focus—film distance was 12 cm; with Agfa Printon Rapid film, an exposure time of 0.7 sec. was required. The photographic film was wrapped in 12 micra thick aluminium foils and placed between the ovary and the supporting table. The microangiograms were obtained during the injection of a contrast medium; the method will be described later. The films were processed in Kodak D. K. 50 developer for 3 minutes, and enlargements obtained by standard photographic and photomicrographic techniques.

In the first series of experiments, a large-bore polythene tube was introduced in a distal direction into the abdominal aorta of untreated anaesthetized rabbits and contrast medium injected under a pressure

varying between 0 and 200 mm mercury. The injection pressure was measured with a mercury manometer which was connected to the aorta distally from the polythene tube. In some cases, the part of the spiral artery visible in the hilum of the ovary was observed in a microscope and photographed; in other cases, microangiograms were obtained. Umbradil 35 % (Astra Chemical Corporation) served as the contrast medium in most experiments, but when many subsequent injections were performed Neo-protosil 20 % (Parke, Davis & Co.) solution was used as Umbradil rapidly diffuses into the tissue and blurs the roentgen films. When Neo-protosil served as the contrast medium, curare was given to the animal to prevent convulsions.

In the second series, microangiograms were taken in the same way as in the first but in rabbits which had been given 200 I. E. gonadotrophin intramuscularly 18 to 72 hours previously.

The animals used in these first two series were sacrificed after the experiments, and the blood vessels of the ovaries were injected with Neo-protosil 20 %. After fixation, stereomicroradiographs were made of the whole ovaries and of thick sections prepared from them (cf. BELLMAN 1953). The ovaries were also examined histologically.

In the third series, microangiography was used to study the same animal and the same ovary before and after the prolonged administration of gonadotrophin. The microangiograms were taken under sterile conditions and Umbradil 35 % used exclusively as contrast medium. The medium was now injected through a 2 mm polythene tube which was introduced into the abdominal aorta from one of the femoral arteries. The abdomen was opened and the ovary exposed for the roentgenography in the same way as in the earlier series. The contrast medium was injected by hand with a 20 ml syringe, and it was easy to see from the blanching of the tissues when the injection pressure was sufficiently high to force the contrast medium into the abdominal aorta and its branches. Eight to ter ml of the contrast medium were used per exposure. In most cases only one microangiogram was made in each experiment but in a few animals three further injections of contrast medium were performed without apparent injury to the animal.

After the experiment, the abdomen of the animal was closed with silk sutures, and the polythene tube was removed from the femoral artery and the vessel ligated.

The animals were then given 200 I. E. gonadotrophin subcutaneously per day for three days and the microangiographic procedure was repeated after five days. A few fragile intraperitoneal adhesions were occasionally observed but they did not interfere with the surgical exposure of the ovary. The animals were sacrificed after the second microangiography, and the actual ovaries were examined in the same way as in the other series.

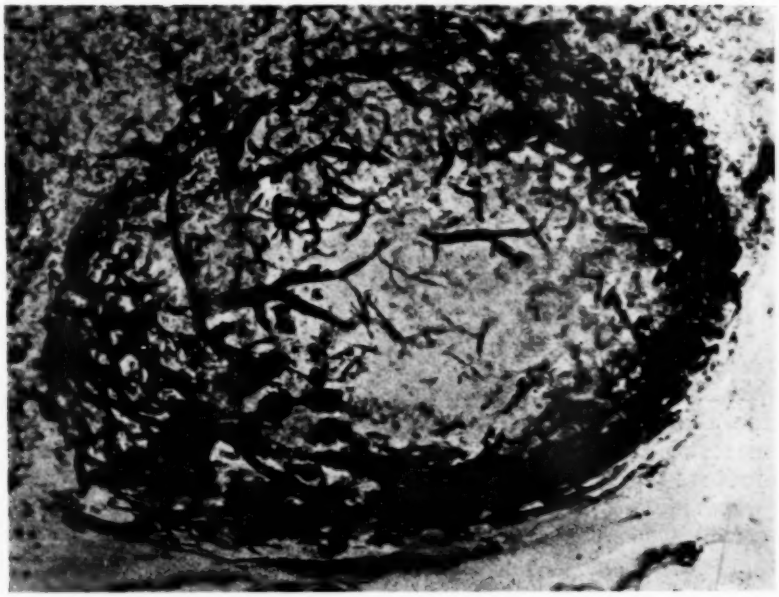

Fig. 1. Microangiogram × 120 from a 200 micra thick section of an ovary from a rabbit not treated with gonadotrophin. The rather sparse capillary net work which surrounds the follicle is seen. The 'top' and the 'bottom' of the capillary clump are cut away.

Results

Microangiograms from fixed thick sections of rabbit ovaries showed blood vessel development similar to that described earlier in albino rats by BELLMAN et coll. (1953): A sphere or rounded clump of anastomosing capillaries develops around the granulosa cell layer as the maturition process starts in the primordial follicles. This blood vessel network is at first sparse but becomes denser during the maturition of the follicle (Figs. 1 and 2). After the rupture of the follicle, large vessels grow perpendicularly from the network (Fig. 3) and a typical anastomosing system of vessels with a diameter of 20 to 30 micra is formed throughout the corpus luteum. The drainage of this blood vessel system is through wide veins which embrace the corpus luteum and appear early in the development of this structure, probably from the capillary system of the ruptured follicle. Microangiograms obtained from living animals (see below) showed that the small arteries leading to these structures increased in size after the administration of gonadotrophin, but no development of new vessels in the stroma of the ovary was observed (Fig. 5).

Fig. 2. Microangiogram × 120 from a 200 micra thick section of an ovary from a rabbit given 200 I. E. gonadotrophin 18 hours before being sacrificed. A fragment of the wall of the follicle with its dense network of anastomosing capillaries. The vascularization is very much greater than in the small follicle seen in Fig. 1.

Vital microscopy during the injection of fluid through the blood vessels of the ovaries of living rabbits showed that an increased injection pressure caused a great increase in the tortuosity of the arteria ovarica and also slight dilation of this vessel. Similar changes were observed in the large veins of the mesovary. Of the arterial spiral in the hilum of the ovary, only the most superficial parts of the coils could be seen by vital microscopy. This indicated that the angle of the spiral decreased slightly with increasing injection pressure and subsequently returned to normal. The smallest blood vessels of the follicles and the stroma could be observed only in the superficial part of the ovary. The filling of the smallest blood vessels was indicated, however, by a white colouring of the organ. This was fragmentary at first, probably because of spasms in the vessels, but increased during the prolonged period of injection of the contrast medium. Homogeneous blanching of the ovary was obtained only when it was irrigated with warm physiologic saline during the injection.

Microangiograms from normal living rabbits showed that both the arteria ovarica and the spiral artery in the hilum of the ovary became slightly dilated when the injection pressure was increased. Sometimes a

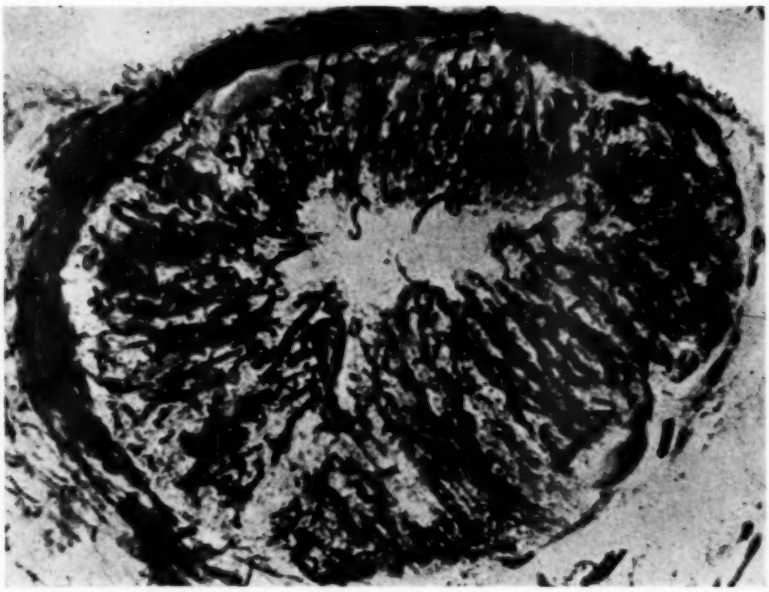

Fig. 3. Microangiogram × 32 from a 200 micra thick section of an ovary from a rabbit given 200 I. E. gonadotrophin 20 hours previously. Young corpus luteum with development of a great number of large vessels perpendicularly from the blood vessel clump remaining from the follicle. (Neo-protosil 20 % was used as contrast medium in the microangiograms of Figs. 1, 2 and 3.)

slight dilatation persisted even after the injection pressure had been decreased. The shape of the spiral in the hilum of the ovary remained unchanged during different injection pressures: no change was seen either in the length, angle or number of coils. The shape of the spiral artery varied considerably among the normal animals; some had a very regular spiral, but in others the shape of the coils varied greatly (Fig. 4). There was no obvious relationship between the type of spiral artery and the macroscopic or microscopic morphology of the ovary. Microangiograms from sections of normal rabbit ovaries showed a rather sparse network of blood vessels in the stroma down to a diameter of about 50 micra. There were usually small follicles in these ovaries, and sometimes both the supply arteries of these follicles and the capillary clump around them could be demonstrated.

Microangiograms from living animals which had been given gonadotrophin also showed that the spiral artery in the hilum of the ovary was rather wide and had irregular coils. The shape of the spiral did not differ from the irregular type of spiral artery seen in normal animals.

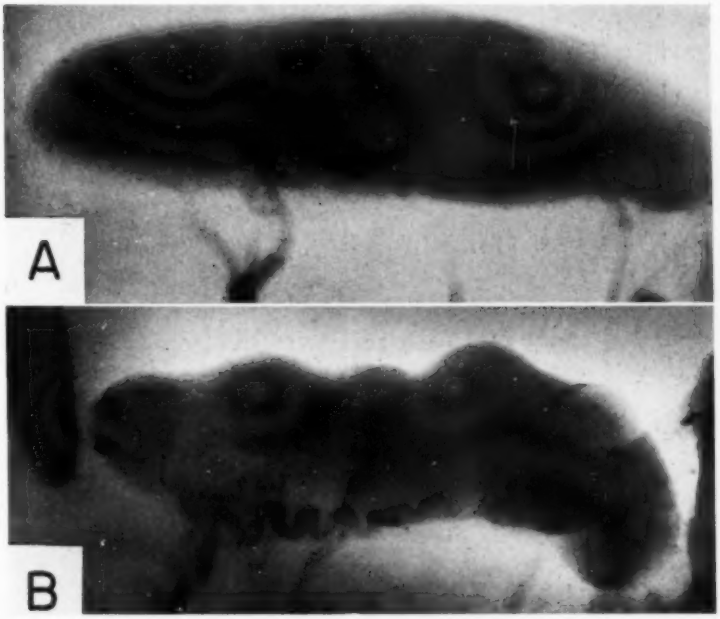

Fig. 4. Microangiograms × 6 from the ovaries of living rabbits not given gonadotrophin. The spiral artery in the hilum of the ovary in the lower microangiogram has regular coils, while the upper artery is rather irregular. Capillary filling of some follicles produces circular shadows.

The films also showed more or less complete contrast filling of growing follicles or young corpora lutea. The rich blood vessel system may be seen in Figs. 2 and 3 which are microangiograms from 200 micra thick sections of these structures.

Microangiograms of the same ovary before and after the administration of gonadotrophin. Before the treatment only small follicles were observed in the ovaries but, following it, many large follicles in the ovaries with diameters up to 7 mm were present. The microangiograms showed that dense capillary spheres had developed round the follicles and that their supplying arteries had increased in size.

The shape of the arteria ovarica varied considerably with the injection pressure applied, as seen in earlier experiments, and therefore no attempts were made to compare the shape of this vessel before and after the administration of gonadotrophin. The spiral artery in the hilum of the ovary also became somewhat wider but no other changes were observed in this vessel. Thus both the shape and number of its coils were uninfluenced by the administration of the hormone.

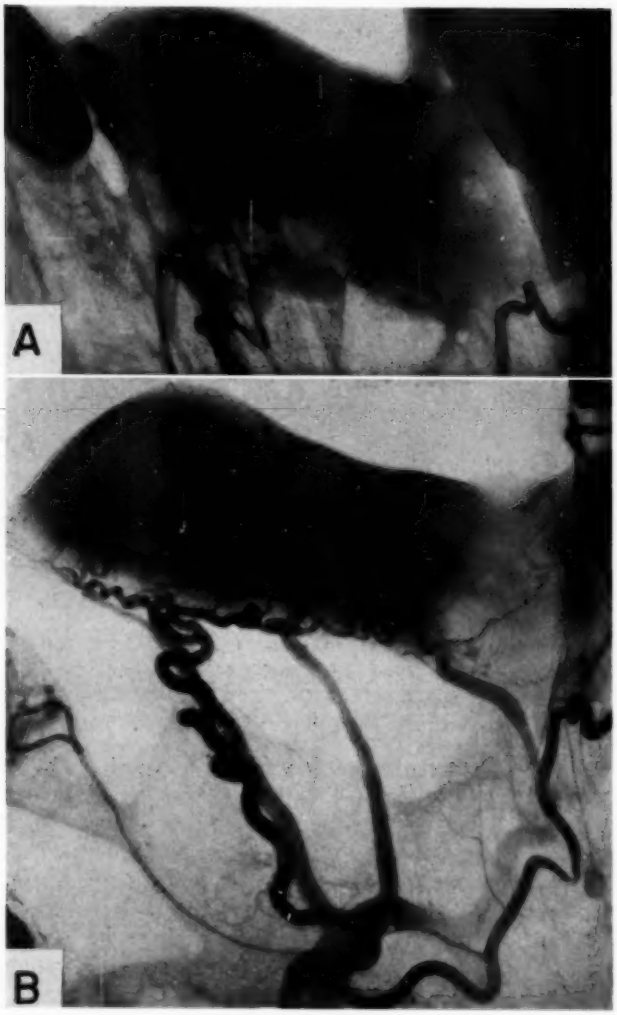

Fig. 5. Microangiograms × 5.5 from the left ovary of a rabbit before (A) and after (B) the administration of 200 I. E. of gonadotrophin subcutaneously for three days; the time interval between the films is five days. The follicles in the ovary before the administration of the hormone cannot be seen in the microangiogram. There is a uniform filling of the vessels in the stroma. The microangiogram taken after the administration of the hormone shows large follicles, the capillary clumps of which produce distinct shadows. The diameter of the supply arteries of the follicles is considerably greater than before the administration of the hormone. The shape of the spiral artery in the hilum of the ovary has not changed during the treatment (the projection differs slightly between the films).

Discussion

It is striking that all arterial vessels of the rabbit ovary are tortuous or even have a pronounced spiral shape. The reaction of these vessels to increased intravascular pressure varies, however, in different parts of the vascular system of the ovary. The arteria ovarica changes its shape greatly for moderate pressure variations, the spiral artery of the hilum only a little, and the small arteries not at all. These differences are probably related to the extent to which these vessels are supported by surrounding ovarian tissue.

The administration of a single dose of gonadotrophin induced the development of large numbers of small blood vessels in the ovaries during the maturition of follicles and development of corpora lutea. The arteries, including the spiral artery in the hilum of the ovary and the arteria ovarica, increased in diameter, but no development of new vessels of this kind was seen. The shape and number of the coils of the spiral artery in the hilum did not change after administration of the hormone. There was thus no indication that the blood supply, and thereby the amount of specific regulatory hormones conveyed to the ovaries, was affected by a direct hormonal influence on the shape of this spiral vessel as suggested by other investigators. The effect on the arteries was similar when giant follicles were produced by prolonged administration of gonadotrophin; it did not seem, in contradistinction to the results reported elsewhere, as if these giant follicles were produced through a changed spiralization of the arteries. The results obtained by REYNOLDS and his co-workers indicated that gonadotrophin increases the blood circulation in the ovaries by extending the coils of its arteries. The experiments described here gave no indication that the spiralization of the arteries of rabbit ovaries was influenced by the administration of gonadotrophin. They also showed that the increased activity which was induced in the ovaries by gonadotrophin included a general expansion of their vascular system. The only change observed in the arteries, and in the veins, was an increase in their calibre. It seems obvious that this is the anatomic indication of an increased blood circulation as it occurs in close relation to the development of vast beds of small blood vessels in follicles and corpora lutea.

SUMMARY

The effect of gonadotrophin on the ovarian blood vessel system in rabbits has been studied by microscopic and microangiographic methods. It was established that the administration of the hormone was followed by an increase in the normal blood circulation, due to dilatation of the finer blood vessels and the afferent arteries. There was no indication that gonadotrophin affected the circulation by changing the spiralization of the arteries.

ZUSAMMENFASSUNG

Die Wirkung des Gonadotropines auf das Blutgefässsystem der Kaninchenovarien ist mit Hilfe mikroskopischer und mikroangiographischer Methoden studiert worden. Es wurde festgelegt, dass die Zuführung des Hormones ein Ansteigen der normalen Blutzirkulation auslöste, welcher auf der Dilatation der feinen Blutgefässe und der zuführenden Arterien beruhte. Nichts deutete darauf hin, dass Gonadotropin die Zirkulation durch Veränderungen der Spirilisation der Arterien beeinflusste.

RÉSUMÉ

L'effet de la gonadotrophine sur le système vasculaire sanguin de l'ovaire a été étudié sur des lapines par des méthodes microscopiques et microangiographiques. Les auteurs ont établi que l'administration de cette hormone est suivie d'une augmentation de la circulation sanguine normale, due à la dilatation des plus fins vaisseaux sanguins et des artères afférentes. Rien n'indique que la gonadotrophine influe sur la circulation en modifiant la spiralisation des artères.

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SOME PRELIMINARY OBSERVATIONS ON THE PROTON MAGNETIC RESONANCE IN BIOLOGIC SAMPLES.[1]

By

Erik Odeblad and *Gunnar Lindström*

If a sample containing atomic nuclei with a magnetic moment is placed in a magnetic field, the nuclei take up certain allowed directions with respect to the field. Transitions between these quantized directions can be induced if electromagnetic radiation with the appropriate quantum energy acts upon the sample. In a magnetic field of about 6,700 gauss the quantum energy for proton transitions is about $9 \cdot 10^{-20}$ erg, corresponding to a frequency of about 26.5 megacycles.

If this 'resonance frequency' is applied to the specimen, and the magnetic field is swept over a small interval less than a gauss, absorption of energy can be detected by the resonance absorption technique of PURCELL,

Fig. 1. Left: the proton signals from water. Right: the proton signals from living yeast cells. The same magnetic field and operating conditions were used in both cases. The magnetic field was swept sinusoidally so that two proton signals appear for each specimen, one at increasing, and one at decreasing, field. The proton signals in yeast were lower and somewhat broader than in pure water.

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TORREY & POUND (1946) or by the nuclear induction technique of BLOCH, HANSEN & PACKARD (1946) as a peak of absorption or 'resonance signal'. This nuclear magnetic resonance signal is highly specific for the nuclei of any particular isotope. Some signals are exemplified in Fig. 1.

The proton magnetic signals in water have been shown to depend upon several important factors. One of these is the presence of paramagnetic substances in solution, which leads to a decrease in the magnetic spin-lattice relaxation time (BLOCH, HANSEN & PACKARD 1946). Furthermore, it is of great importance that the relaxation time decreases if the viscosity of the sample increases (BLOEMBERGEN, PURCELL & POUND 1948). An important observation, first made by ROLLIN (1946), is that the signal is considerably broadened and lowered upon crystallization to ice. A broadening also occurs following adsorption of water on 'hygroscopic' material (SHAW & ELSKEN 1953). If the nuclear magnetic resonance signal can be studied at high resolution, there is often a splitting or shift due to chemical effects (SIEGBAHN & LINDSTRÖM 1949, LINDSTRÖM 1950).

In biologic samples, rather complicated phenomena due to the viscosity, presence of paramagnetic enzymes, water adsorption on proteins etc., predominate. It therefore seemed to be of interest to obtain information concerning certain characteristics of the proton magnetic resonance in biologic objects. In the present work, we have examined the proton signals at low resolution on living cells and other biologic samples.

Experimental

We have used a magnetic resonance absorption set-up, described in detail by LINDSTRÖM (1951). The magnetic field strength has been about 6,700 gauss and the radiofrequency about 26.5 Mc/sec. The radiofrequency bridge for detection of energy absorption was balanced as carefully as possible and the signal from the bridge demodulated in a radio receiver, amplified and displayed on a cathode ray oscilloscope screen, and recorded photographically; in a few cases it was measured directly on the screen. The width of the resonance peaks was about $1:10^5$, limited mainly by inhomogeneities in the magnetic field. Splitting, shift, or other fine structure, of the signal has therefore usually not been possible to observe. The signal-to-noise ratio varied between about 50:1 and 10:1. The samples were placed in sealed ampullas of 2.8 ml or in large sealed test tubes. All the measurements were undertaken at + 18° to + 20° C.

In measuring the relative *size* of the proton magnetic resonance signals, the operating conditions, such as the output from the generator, the bridge balance etc., were kept constant throughout the run and the signals were photographed and the areas measured planimetrically in pictures. The

error in a single measurement of this kind was judged to within about 9 per cent. Photographs also enabled observation on the *width* of the signals.

In measuring the *relaxation time*, the specimen was saturated by a strong radiofrequency field which was suddenly decreased and the growth of the height of the signal recorded on moving film. The errors in measuring relaxation times in this way are probably fairly great and difficult to decide, especially as the 'relaxation time' may be composed of several components. If there is one component we estimate the error in relaxation time to within + 35 and — 25 per cent. Relaxation times shorter than about one second cannot be measured with this technique.

Results

In a first series of experiments, the signal size was measured for distilled water which had been aerated for two hours with nitrogen, air or oxygen. As shown in Table 1, there was no measurable difference

Table 1.

A	B	C	D	E	F
Dist. water under N_2	13.4	0.7	10	94	100
Dist. water under air	14.2	0.6	11	100	100
Dist. water under O_2	14.8	0.7	10	106	100

Key to columns in Tables 1, 2, 3 and 5.
A = Specimen observed. B = Relative area (or height) of resonance signal. C = Standard error in B. D = Number of observations to find value of B. E = Area of signal, that of (first) water sample in the series = 100. F = Water content from drying and weighing.

between the three groups of specimens (which might have been expected, CHIAROTTI & GIULOTTO 1954). We concluded that biologic changes in the atmosphere above the specimen were of minor importance in the investigations which followed.

Table 2.

A	B	C	D	E	F
Dist. water	11.5	0.4	12	100	100
Physiol. saline	11.7	0.5	12	102	99
Heparin 1 %	11.4	0.4	12	99	99
Human blood serum	10.6	0.4	10	92	93
Rabbit blood serum	10.4	0.5	10	90	93
Human red blood cells	9.5	0.5	10	83	64
Living yeast cells	9.6	0.4	11	84	69
Killed yeast cells	9.0	0.5	12	78	70
Dist. water	11.2	0.5	11	97	100

In the next series, the size of the resonance signal was compared for distilled water, physiologic saline solution, 1 per cent heparin in distilled water, human serum, rabbit serum, living human red blood cells and living and killed (with NaF) yeast cells. The results are shown in Table 2 in which the water contents for some of the material are also given, as measured by drying at + 110° C. The signals for the yeast cells (both living and killed) appeared to be somewhat broader than for pure water.

In a third series of experiments, the size of the signals was measured for distilled water, liver, striated muscle and fat tissue removed immediately after death from rabbits or rats. These results are shown in Table 3.

Table 3.

A	B	C	D	E	F
Dist. water	36	3	8	100	100
Rabbit liver	27	4	9	75	70
Rabbit str. muscle	25	3	9	63	66
Rabbit fat tissue	51	6	11	142	34
Dist. water	34	4	8	94	100
Dist. water	40	4	6	100	100
Rat liver	31	3	5	77	72
Rat str. muscle	29	3	4	72	68
Rat fat tissue	59	5	7	147	37
Dist. water	39	4	5	98	100

As seen from these results, the signal size was about proportional to the water content except for fat tissue where it considerably exceeded the water content.

In a fourth series of experiments, we measured the relaxation times for protons in distilled water, glycerine (as standard), liver, striated muscle and fat. The values obtained of the relaxation time are shown in Table 4.

Table 4.

G	H	J	K
Dist. water	1.9	0.4	5
Rabbit liver	2.2	0.5	4
Rabbit str. muscle	1.7	0.4	4
Rabbit fat tissue	<0.8	0.2	5
Glycerine	<0.8	0.2	5
Dist. water	1.7	0.4	4
Calf cartilage	<0.8	0.2	4
Human tendo Achillis	<0.8	0.2	4
Dist. water	2.0	0.3	8
Heavy water, 60 %	3.2	0.6	7

Columns in Table 4: G = Specimen observed. H = Relaxation time in seconds. G = Estimated error in H. K = Number of measurements.

Table 5.

A	B	C	D	E	F
Dist. water	22	4	4	100	100
Cartilage	26	3	6	118	53
Fibrous tissue	22	5	5	100	42
Corpus vitreum	20	4	4	92	97
Dist. water	23	3	4	104	100

In a fifth series, we measured the signals from distilled water, calf cartilage 6 hrs post mortem, human fibrous tissue (tendo Achillis) 6 hours post mortem and rabbit corpus vitreum (2 hours post mortem). The signal heights are given in Table 5. Though no measurements could be performed we observed a much shorter proton relaxation time (< 0.8 sec.) in cartilage and fibrous tissue than in water.

In a sixth series of experiments, we exchanged the water in red blood cells with heavy water and studied the size of the proton signals. The results are shown in Diagram 1. We also made a calibration curve of the proton signals at different atom percentages of heavy and common water as shown in Diagram 2. We found a correlation line which might be slightly

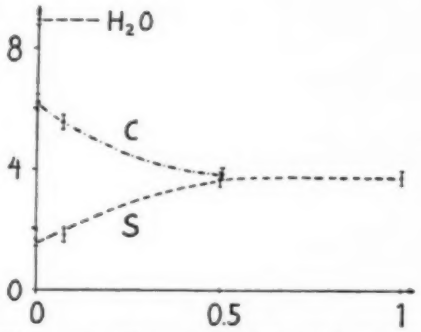

Diagram 1. The results of the exchange of water with deuteriumoxide in red blood cells. Ordinate: Area of signal. Abscissa: time in hours after introducing the 'physiologic' 70 per cent heavy water in the sample of red blood cells. C denotes the curve for red blood cells, separated by centrifugation and S the curve for the corresponding supernatant serum.

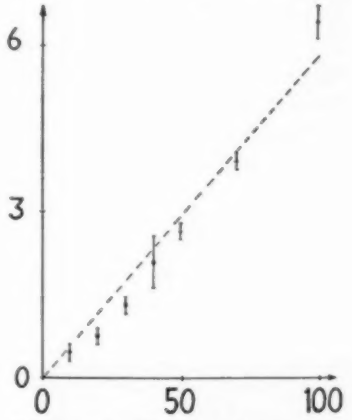

Diagram 2. Relation between the area of the signal and the isotopic percentage of hydrogen in mixtures of water and heavy water. Each value represents the mean value and mean error for 5 to 9 determinations.

curved. The proton relaxation time was also measured in common water and 60 per cent heavy water and the values shown in Table 4 were obtained.

Discussion

The present work has shown that proton magnetic resonance signals may readily be obtained from living cells and other biologic tissues. In spite of the complicated conditions prevailing in biologic tissues, the size of the proton magnetic resonance signals sometimes corresponded fairly well to the total amount of water present in the tissue but, at others, this was not the case. In fat tissue the signal was much larger. We ascribe this to the presence of protons in fat bound to the carbon chains in fat molecules. The relaxation time in fat tissue also seemed to differ from that in the other tissues investigated. In cartilage and fibrous tissue, in which the proton signals probably arise from highly viscous water with short spin-lattice relaxation time, the signals were also larger than would correspond to the water content. The relaxation time is, however, as mentioned above, an ill-defined property since there may be several components of different relaxation times in tissues.

On the basis of the work of SHAW, ELSKEN & KUNSMAN (1953) and JACOBSON, ANDERSON & ARNOLD (1954), one might expect some of the tissue water to be adsorbed on proteins or organized in an ordered lattice due to intracellular nucleic acids, thus decreasing the size of the observed resonance signals. Such a decrease has not been possible to detect with certainty in the present work, which may, however, be due to the rather great method error and other factors affecting the signal size. The protons bound in proteins and many other organic compounds (not including fat) may probably give resonance signals which are so broad (SHAW & PALMER 1951, SHAW, ELSKEN & KUNSMAN 1952, SHAW, ELSKEN & PALMER 1952) that they would not appear on the oscilloscope screen in the present work.

We hope to be able to re-examine and extend this work later, using refined methods, including high-resolution and spin-echoes, for more careful measurements of signal size, fine structure and relaxation times. We believe this will give valuable information of a biologic and physical nature.

SUMMARY

The proton magnetic resonance signals were studied at a resolution of about 1: 10^5 at 26.5 Mc/sec. in a number of biologic samples including fat tissue, cartilage and fibrous tissue, etc. Excessively high proton signals, compared to their water content, were noted in these tissues; this might be due to the relationship of the protons bound in fatty acid chains in fat tissue and to the high viscosity of water in cartilage and fibrous tissue. The

proton relaxation time also seemed to be considerably shorter than in water. The exchange of water with deuteriumoxide was studied in red blood cells by means of proton magnetic resonance. Proton signals in mixtures of deuteriumoxide and water were also investigated.

ZUSAMMENFASSUNG

Die Protonresonanzsignale sind bei einer Auflösung von etwa 1: 10^5 bei 26.5 Mc/Sek. in einer Anzahl biologischer Proben von Fettgewebe, Knorpel und Bindegewebe, etc. untersucht worden. In diesen Geweben wurden im Verhältnis zu ihrem Wassergehalt ausserordentlich hohe Protonsignale beobachtet. Dieses mag auf den Beziehungen der im Fettgewebe in Fettsäureketten gebundenen Protonen und der hohen Viskosität des Wassers im Knorpel und im Bindegewebe beruhen. Die Relaxationszeit der Protone scheint hier auch erheblich kürzer zu sein als in Wasser. Der Austausch von Wasser mit Deuteriumoxid wurde mit Hilfe von magnetischer Protonresonanz in roten Blutkörperchenzellen studiert. Protonsignale in Mischungen von Deuteriumoxid und Wasser wurden ebenfalls untersucht.

RÉSUMÉ

Les auteurs ont étudié les signaux de résonance protonique avec une résolution d'environ 1: 10^5 à 26.5 Mc/sec. sur un certain nombre de préparations biologiques comprenant du tissu adipeux, du cartilage, du tissu fibreux, etc. Ils ont observé sur ces tissus des signaux protoniques excessivement élevés par rapport à leur contenu en eau; ceci pourrait être dû à la relation entre les protons liés dans les chaînes d'acides gras du tissu adipeux et la haute viscosité de l'eau dans le cartilage et le tissu fibreux. Le temps de relaxation protonique a paru lui aussi considérablement plus court que dans l'eau. L'échange entre l'eau et l'oxyde de deutérium a été étudié sur des globules rouges grâce à la résonance magnétique des protons. Les auteurs ont aussi étudié les signaux protoniques dans des mélanges d'oxyde de deutérium et d'eau.

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A METHOD FOR THREE-DIMENSIONAL DOSE-FINDING IN TELERADIUM THERAPY

by

Rune Walstam

As early as 1921, teleradium therapy was introduced at Radiumhemmet by BERVEN (4, 5). During the subsequent years, various types of apparatus for treatment have been in use at the clinic (LYSHOLM 9, SIEVERT 13, BENNER 1, 2, 3).

On the basis of clinical experience and with the aid of dosage measurements (SIEVERT 12) and dosage calculations, the therapeutic technique has undergone further development.

At Radiumhemmet, as at other clinics, greater efforts have been made in recent years to obtain more exact knowledge of the dosage distribution in the treatment zone. An attempt is made to give quantitative physical precision to the clinical experience at Radiumhemmet. In addition to the use of such devices as a dose-contour projector (MAYNEORD 10), we have applied an entirely new method in multiple-field treatment with teleradium. A brief account of this method is given in the following.

The Treatment Method. According to the practice developed at Radiumhemmet (BERVEN 5, 6, and JACOBSSON 7), carcinomas of the oral cavity are treated chiefly with teleradium, electroendothermy and surgery. Multiple field radiation is given to the primary tumour and to the metastases, and any tumour remains are treated with electroendothermy. Operable metastases are treated by dissection.

Treatment is most often given with a 5-gramme radium bomb; the dosage distribution is shown in Fig. 4. This usually results in a satisfactory homogeneous dose to the primary tumour and metastatic areas.

The multiple field technique, with the central axes of the fields placed at fixed distances apart and arrranged to give the necessary dose distribution, is based on:

a) homogeneity with two parallel fields with centre axes at about 7 cm distance (Diagram 1 a). (With a shorter distance, a region of maximum

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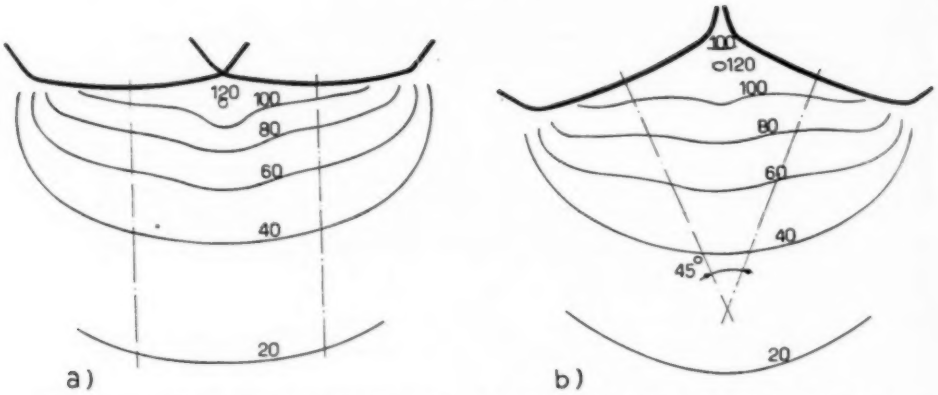

Diagram 1. The dosage distribution with two teleradium fields with axes about 7 cm apart.

a) central axes parallel; b) central axes non-parallel (45° angle between axes).

dosage, with a risk of necrosis, is obtained between the two fields; with a greater distance, there is a maximum dose at the centre of each field.)

b) transformation of this principle to non-parallel axes depending on the roughly spherical isodose surfaces at the depth used (2—5 cm). This fact is evident from Diagram 1 b and clinical experience has shown that this rule of thumb applies with a good degree of approximation (JACOBSSON 7).

The dosage. The dosage in teleradium therapy was earlier stated in Imc-hours, a unit introduced in 1931 by SIEVERT (11, 14). Nowadays, the dosage is stated in international r units. The conversion factor 1 Imc-hr = 7.5 r is found in many of the publications from Radiumhemmet. It was, however, changed on 1 January 1952 to *1 Imc-hr = 8.3 r* which is in better agreement with the conversion factors most commonly used internationally.

Principle of the Method. The essential feature is a wire jig, which is constructed individually for each patient for whom such dosage calculations are to be made. Since the wire is pliable, the jig can be shaped to conform closely to the surface of the skin in the treatment zone. Consequently, it may be used as a basis for a three-dimensional picture of this zone.

Movable indicators are attached to the jig; they mark points of interest for the dosage calculations, *e. g.* a certain point in the tumour, or any metastases present. The jig is also provided with 'centre axes', which afford suggestions for the placing and direction of the central rays of the teleradium fields.

a. b.

Fig. 1. The primary tumour. a) at the beginning of treatment; b) five months after the radiation treatment.

There is circular symmetry in the dosage distribution of the teleradium apparatuses at Radiumhemmet. The dosage contribution from a certain treatment field in each calculation point may therefore be obtained by placing an isodose diagram over the 'centre axis' of the treatment field, and rotating it about this axis.

When the calculations have been completed and the dosage has been fixed, the wire jig is used as a directional device.

In order to demonstrate the performance of a dosage calculation, I have taken a concrete case, a patient with carcinoma of the right side of the tongue. (The dosage calculations were made in collaboration with Ass. Professor FOLKE JACOBSSON (8), who is responsible for the clinical data in this paper.)

Case report. The patient was a 67-year-old man. A primary tumour of the squamous-cell type, measuring about 3.5 by 2 cm, was present on the right lateral and lower parts of the tongue (Fig. 1). Palpation showed that it did not extend far back into the base of the tongue. The consistency of the tumour was firm to hard; biopsy showed it to be a fairly highly differentiated, slightly cornified squamous-cell carcinoma.

In the posterior part of the carotid triangle, below the sternocleidomastoid muscle, a fixed metastasis, 2.5 by 3 cm, was palpable; it was verified by needle biopsy. Another metastasis, about 8 mm in diameter, was palpable below the right margin of the mandible; a similar, slightly smaller lymph node was palpable on the left side as well.

Dosage Calculations. In collaboration with the physicians and physicists, the skin markings representing the centres of the treatment fields were made at distances of 6.5

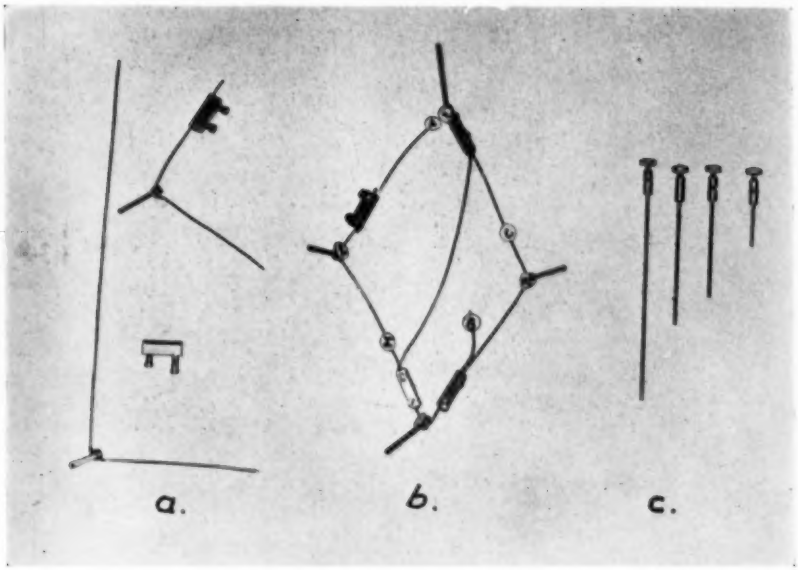

Fig. 2. Details of the wire jig: a) angle joints and braces; b) assembled jig; c) indicators to be fixed on the wire jig and showing the points for which calculations are to be made. Note centimeter markings.

cm apart. These markings usually form a triangle or quadrangle, which is designed to cover the areas to be irradiated as satisfactorily as possible.

The wire jig is constructed in accordance with the treatment zone charted. The jig is made of cold-drawn brass wire, 1 mm in diameter for the 'ribs' which are bent to fit the skin surface, and 2 mm in diameter for the 'centre axes' giving the direction for the central rays of the treatment fields.

The wire can easily be shaped manually, and it has sufficient stability and elasticity to withstand normal strains. (For the adjustment of the teleradium apparatus, see the following.)

As a rule, the jig is assembled by means of 'angle joints', prepared in advance (see Fig. 2). A 'centre axis' is soldered to two 'ribs'. Such a joint is placed at the centre of each proposed field; the 'ribs' are then bent to conform to the skin surface and point to the centre of two other fields. The angle joints are assembled with the help of small braces. Since they form part of the standard equipment in electric coupling material, they are relatively inexpensive.

The direction of the 'centre axes' is adapted to the requirements for the position of the volumes of maximum dosage. A dummy of the treatment bomb is then used to test the possibility of applying the directions suggested to the patient.

When four fields are used, it is often desirable to reinforce the jig with a diagonal strut.

Fig. 3 shows the jig in position on the patient under discussion.

The points in the treatment zone for which dosage calculations are to be made are selected in consultation between the radiologists and physicists. Due consideration is

Fig. 3. The wire jig in position on the patient, and provided with indicating points for dosage calculations.

then paid both to the clinical requirements for the dosage and to the risk of hot spots. In the case in question, the following points were chosen (*cf.* Fig. 3).

A. A point on the skin immediately above the centre of the primary tumour. At this point, the dose is calculated at each cm of the depth, down to the medial part of the tumour.

B. A point on the skin immediately above the palpable metastasis, of which the greatest depth is assumed to be less than 3 cm. In the present case, this is presumably the point of maximum dosage.

C. A point on the skin immediately above the suspected submandibular lymph node, which is considered to lie at a depth of 2 cm.

M. A point above the medulla which, in this case, lies about 6 cm below the 'plane' of the jig.

The skin dose is always calculated for the centre of each field and for other points at which a risk of hot spots may reasonably be anticipated to occur.

In determining the points for calculation, it is often useful to take a roentgenogram of the treatment zone with the patient in the position he will occupy during treatment and with the jig in place.

A number of movable indicators (Fig. 2) are attached to the jig to mark the points in the treatment zone for which calculations are to be made. The isodose diagram is fitted with a tubular guide (Fig. 4); it is placed over each of the 'centre axes' on the jig and rotated about them, so that the dose contribution at a given point may be read off as a percentage of the dose given to the relevant field (Fig. 5). The isodose curve is placed over each of the 'centre axes' of the jig in turn, and the dose contribution at the points marked is read off. The results of the readings in the present case are assembled in Table I.

The data in the table are used for more or less detailed charting of one or several schemes of treatment. It is then simplest to make the first approach under the conditions of an equally large direct skin dose to all the fields.

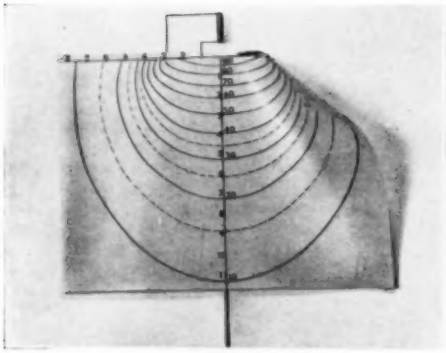

Fig. 4.

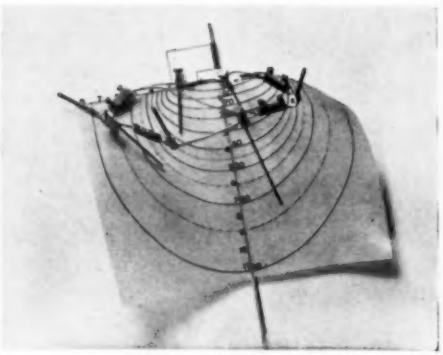

Fig. 5.

Fig. 4. Isodose diagram drawn on transparent, flexible paper and provided with tubular guide for the 'centre axis' on the wire jig. The 5-gramme teleradium bomb without lead cone in use at Radiumhemmet has a field 6 cm ⌀ and a radium—skin distance = 6 cm. The intensity extrapolated to the surface is fixed at 100 (BENNER 2).

Fig. 5. The isodose curve placed over the centre axis of Field 3. The dose contribution from this field is read off:

at	point	A_3	as	21	per	cent
»	»	A_4	»	23	»	»
»	»	C_2	»	58	»	»
»	»	M	»	16	»	»

If it is assumed in the present case that a direct skin dose of 4,000 r is given to each field, the dosage distribution shown in the column of Table II entitled 'Treatment Scheme I' is obtained. The maximum dose, 6,440 r, is then obtained at point B_0, whereas the centre of the primary tumour, A_3, receives only 4,400 r, or 68 per cent of the maximum dose.

According to Table I, the centre of the primary tumour, A_3, receives the largest dose contribution from Treatment Field 1. This gives, however, a small contribution at point B_0 and, since the skin dose at point F. 1. is approximately 1,100 r less than at B_0, it should be possible to increase the dose to Field 1. The following dosage is denoted as Treatment Scheme II:

Field 1: 5,200 r direct skin dose.
Fields 2—4: 4,000 r » » » .

The dosage distribution obtained is seen in the column of Table II entitled 'Treatment Scheme II'. With this scheme, the centre of the primary tumour receives 5,000 r, or 76 per cent of the maximum dose, 6,600 r. These doses are delivered in an overall time of about 18 days.

A comparison between the two schemes of treatment thus shows that the second scheme gives a dose to the centre of the primary tumour which is 600 r more than that in the first scheme, whereas the maximum dose is increased by only 160 r. The advantages of Scheme II are, however, slightly decreased by the biologic effect of the greater volume dose.

Table I

Reference point (cf. jig Fig. 3)	Depth cm	Denotation	Dose contribution in % of *direct* skin doses, from field: 1	2	3	4
A	1	A_1	78	24	18	8
»	2	A_2	62	28	19	9
»	3	[1]) A_3	49	30	21	10
»	4	A_4	40	29	23	12
B	0	B_0	14	22	85	40
»	1	B_1	15	24	71	42
»	2	[2]) B_2	15	26	57	41
»	3	B_3	15	25	47	37
C	1	C_1	40	19	76	14
»	2	C_2	41	21	58	15
»	3	C_3	40	23	48	17
M	6.5	M	13	15	16	23
1	0	F. 1.	100	15	13	6
2	0	F. 2.	17	100	14	13
3	0	F. 3.	18	13	100	20
4	0	F. 4.	8	13	15	100

underlined numbers: cf. Fig. 5.

[1]) centre of primary tumour.
[2]) centre of metastasis.

The above is quoted as an example of the way in which the data in a dosage calculation are used. The closer the contact between the clinicians and the physicists, the more valuable will be the information obtained for the treatment in the individual case.

Starting from the clinical requirements, and using the dosage calculations as a basis, a preliminary dosage is decided on. The individual variability of the clinical course usually necessitates subsequent deviations from the preliminary dosage. It is easy with the help of Table I to calculate, during the course of treatment, the doses obtained with the changes in the dose to the given fields, or to study the changes in the dosage distribution resulting from the introduction of new fields of treatment. In the latter case, additional 'centre axes' representing the proposed fields of treatment are attached to the wire jig.

Irradiation. When the scheme of treatment has been fixed, the wire jig is used as a *directional device*, as shown in Fig. 6. Of course it is then used only for setting of the correct direction of the central beam. When the angulation of the apparatus has been set with the help of the wire jig, the latter is removed. The apparatus and the patient are then moved so that the front of the apparatus lies in contact with the skin in the centre of the treatment field.

The wire jig is easy to use as a directional device, and ensures a satisfactory degree of accuracy when the treatment apparatus has a dosage distribution without sharply delimited fields.

Primary Treatment Results. The final result of treatment in this case, selected for demonstration of the dosage calculation, cannot of course be ascertained as yet. The course of the reactions has, however, proceeded normally in the manner described by JACOBSSON (7).

Table II

Calculation point	Treatment Scheme I		Treatment Scheme II	
	Dose r	Dose in % of max. dose	Dose r	Dose in % of max. dose
A_1	5,120	80	6,040	92
A_2	4,720	73	5,480	83
A_3	4,400	68	5,000	76
A_4	4,160	65	4,640	70
B_0	6,440	100	6,600	100
B_1	6,080	94	6,280	95
B_2	5,560	86	5,740	87
B_3	4,960	77	5,160	78
C_1	5,960	93	6,440	98
C_2	5,400	84	5,880	89
C_3	5,120	80	5,600	85
M.	2,680	42	2,840	43
F. 1.	5,360	83	6,560	99
F. 2.	5,760	90	5,960	91
F. 3.	6,040	94	6,240	95
F. 4.	5,440	85	5,540	84

Treatment Scheme I: 4,000 r direct skin dose to each field.

Treatment Scheme II: 5,200 r direct skin dose to Field 1. 4,000 r direct skin dose to Fields 2, 3, and 4 (about 1,000 r surface dose daily to one field only).

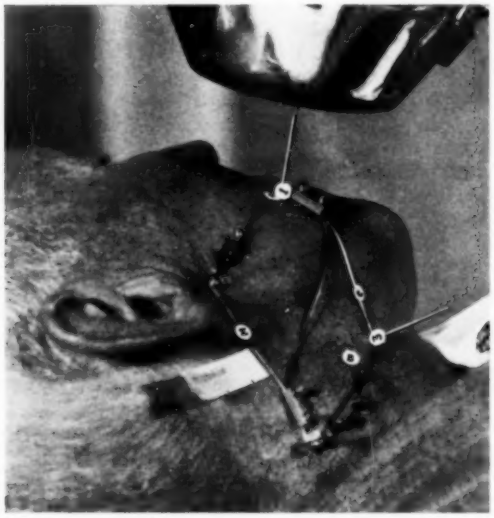

Fig. 6. The wiré jig in use as a directional device.

The radiation treatment was given in an overall time of 19 days. The primary tumour was radiosensitive and disappeared with the given dose, which is calculated to be 5,100 r in the centre of the tumour, without the need of electroendothermy.

The inoperable fixed metastasis (point B_1) was given about 6,700 r. It then became movable and decreased appreciably in size. There were pronounced microscopic changes when it was removed at neck dissection two months after the irradiation. The metastasis at point C showed a similar microscopic picture.

Discussion

It may be inferred from the example given that the wire jig is useful for practical dose-finding, and as a directional device in therapy of the type in use at Radiumhemmet for the treatment of tumours of the oral cavity and the neck.

A great advantage of the method is its simplicity, which allows calculations of the type described to be made in about 3 hours. Consequently, it has been possible to make such calculations in almost every case of this kind that has been treated at Radiumhemmet during the past two years.

The wire jig makes it possible for us to reconstruct a given treatment even years after the irradiation of the patient has been carried out.

The method is used only in treatment with three or more fields, all of which do not lie in the same plane. When all the treatment fields are co-planar, isodose curves are easily obtained with the usual techniques. The method in question functions satisfactorily when there is circular symmetry in the dosage distribution, and provided that rotation of the isodose diagram is not hampered by the jig or by the indicators attached to it. In certain cases it has proved satisfactory to use isodose diagrams from which pieces have been cut out, or to have only a few of the points drawn in at each series of readings.

With some modification, it should be possible to use the method for fields without circular symmetry of the dosage distribution. It would then be suitable to construct the 'axes' of the wire jig in the form of tubes, to be used for steering isodose curves of the type described by WILSON (15). Calculations with jigs of this modified type are intended for use with the Co^{60} bomb which will be installed at Radiumhemmet. This apparatus will be provided with diaphragms for different treatment fields and tubes for treatment at varying distances.

SUMMARY

An attempt is made to give quantitative physical precision to the clinical experience with teleradium therapy at Radiumhemmet. The principles of the standard multiple field technique are discussed. A description is given of a simple wire jig which has been found useful both for dose-finding and as a directional device for

beam alignment. An example is given of its practical application in the treatment of a typical case of carcinoma of the tongue.

ZUSAMMENFASSUNG

Es wird eine Methode für dreidimensionelle Dosisberechnungen bei Teleradiumtherapie beschrieben. Die Prinzipien der am Radiumhemmet verwendeten Mehrfelder-Technik werden diskutiert. Eine einfache Richtanordnung aus Draht hat sich als sehr nützlich für die bestimmung der Einstrahlrichtungen und der Dosen erwiesen. Als Beispiel wird die praktische Anwendung bei der Behandlung eines typischen Zungenkarzinomes geschildert.

RÉSUMÉ

L'auteur s'est efforcé d'apporter une précision quantitative physique à l'expérience clinique acquise à Radiumhemmet en matière de télécuriethérapie. Il étudie les principes de la technique standard à champs multiples. Il décrit une simple grille de fils métalliques qui s'est montrée utile pour déterminer la dose et comme dispositif de centrage pour la direction du faisceau.

Il donne un exemple de son utilisation pratique dans le traitement d'un cas typique de cancer de la langue.

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ANALYSIS OF GAS MIXTURES BY MEANS OF BETA RAY TRANSMISSION MEASUREMENTS[1]

by

Åke Norhagen and *Erik Odeblad*

When beta rays from a radioactive source pass through a gas, their attenuation or absorption takes place due to the stopping and scattering of the individual beta particles by the gas. These effects depend in the first approximation on the total number of electrons passed by a fixed beam of beta particles. It therefore seems likely that gases of the same pressure and temperature but with different molecular electronic numbers would exhibit different transmission constants for beta rays. We have examined this question and found that the expected differences exist and that they are of such a magnitude that gas analysis under certain conditions, as will be discussed later on in the present paper, may be based upon this phenomenon.

Theoretical aspects

Consider a point source of beta radiation at a distance D from a radiation detector (most conveniently a Geiger-Müller tube). The impulse rate in the detector i is then

$$i = I \cdot T(D)/D^2 \quad \ldots\ldots (1)$$

$T(D)$ being the transmission function. As only the first part of the transmission curve, in the main, is utilized in the present work, the approximation that it is an exponential function (Siri 1949), may be justified, so that we may write:

$$i = I \cdot \exp(-\mu D)/D^2. \quad \ldots\ldots (2)$$

A continuous function of another type has been given (Odeblad 1955) to account for the whole course of the absorption curve and may be applied in more careful work. In these equations I is the impulse rate at unit distance without any absorption. If equation (2) is written in logarithmic form we obtain:

$$\log i = \log I - \mu D \log e - 2 \log D. \quad \ldots\ldots (3)$$

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In a gas mixture of several components 1, 2, 3 etc. the total absorption coefficient μ is composed of the individual mass absorption coefficients μ_1, μ_2, μ_3 etc., which add up to form μ since the interaction of the beta particles with the molecules of gas 1 is mainly independent of the interaction with the molecules of the gas 2, gas 3 etc. We may therefore write:

$$\log i = \log I - 2 \log D - 0.4343 D (p_1\mu_1 + p_2\mu_2 + p_3\mu_3 + \ldots) \ldots\ldots\ldots (4)$$

where p_1, p_2, p_3 etc. denotes the partial pressures (in units of one) of gas components 1, 2, 3 etc.

Because the attenuation of beta rays is effectuated mainly by collision with atomic electrons (for light elements) it is reasonable to assume that the absorption coefficient (μ_1, μ_2, μ_3, ...) is roughly proportional to the molecular electronic number, because the number of gas molecules in a given volume is proportional to the partial pressure. Mass absorption coefficients for various elements and chemical compounds have been given and discussed by WESTERMARK (1949, 1954).

If we consider the simplest case where we have a mixture of two gas components 1 and 2, we may write eq. (4) as follows:

$$\log i = \log I - 2 \log D - 0.4343 D [p_1\mu_1 + (1 - p_1) \mu_2],$$
$$\text{or } \log i = \log I - 2 \log D - 0.4343 D [\mu_2 + p_1 (\mu_1 - \mu_2)]. \ldots\ldots\ldots (5)$$

This equation implies that there should be, in the first approximation, a linear relationship between the logarithm of the impulse rate and the partial pressure of each of the components of the binary gas mixture at a fixed distance between source and detector.

According to eq. (4) a constant gas mixture, e. g. normal air, may, in a physical respect, be treated as a single gas in this work.

In a more careful theoretical analysis, detailed consideration has to be given to the variation of the electronic absorption coefficient with binding energy, nuclear scattering of beta particles, geometrical effects, the deviations from the exponential approximation discussed above, as well as certain other matters. These considerations were regarded unnecessary in the present preliminary interpretation.

Experimental

The radioactive isotope S^{35} employed forms a cheap and convenient source of beta radiation. It has a maximum energy of 0.16 MeV and the shape of the beta spectrum is of an allowed shape so that the first part of the transmission curve is nearly exponential with a half-value at about 4 mg/cm² of matter. The distance D has been 7.1 or 9.3 cm. The strength of the S^{35} source was about 25 μC or 80 μC. The Geiger-Müller tube had a mica end-window of about 3.5 mg/cm². One drawback of the S^{35} source is the short half-life (87.8 days). A C^{14} source (0.16 MeV, 5,580 years half-life) could be used to avoid this. The construction of the gas chamber is shown in Fig. 1.

Gas mixtures of known composition were used. The rate of flow in cm³/sec. of each gas at actual barometric pressure and temperature was measured volumetrically by the water displacement method. The gases of bombs manufactured by the AGA Company were used. Impurities up to 3 per cent might be present; these amounts were of little significance in

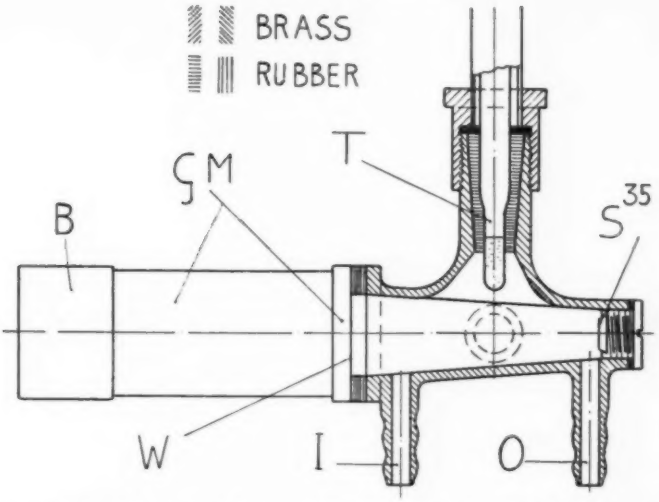

Fig. 1. Cross-section of the chamber used for beta ray transmission measurements of gases. S^{35} = source of beta radiation, GM = Geiger-Müller tube, B = socket of Geiger-Müller tube, W = window of Geiger-Müller tube, I = gas inlet, O = gas outlet, T = thermometer.

the present work, since, in every case, a constant gas mixture was present. The Geiger-Müller countings were undertaken so that the statistical error of every counting was less than 1 per cent (> 10,000 impulses counted). The temperature in the gas chamber was 23° to 25° C in these measurements.

Results

Results of measurements on mixtures of He and O_2, He and N_2, N_2 and O_2, He and air are given in Diagrams 1, 2, 3, 4 and 5.

The results showed that there exists, in the first approximation, the theoretically expected approximately linear relationship between the logarithm of the impulse rate and the partial pressure of one gas component in a binary mixture. There was probably, however, a slight deviation from the linear relationship. The differences in counting rate were so great that no difficulties seem to exist, in principle, in analysing gas mixtures of two gases with an accuracy of one per cent. The uncertainty in the composition of the gas mixtures was greater than the counting error, due to the volumetric error which was of the order of the size of 1.9 to 2.8 per cent in the present investigation. No reliable corrections for coincidence losses could be made.

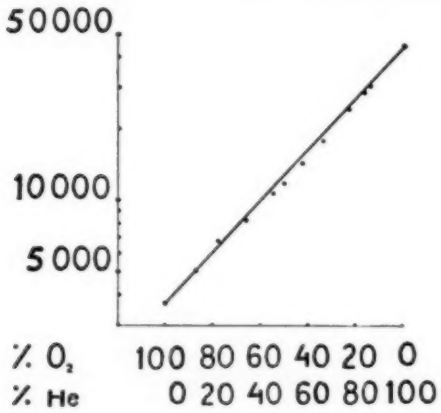

Diagram 1. The relation between the number of counts per minute (logarithmic ordinate) and the volumetric percentage of helium and oxygen. Chamber length = 7.1 cm, source = about 25 μC.

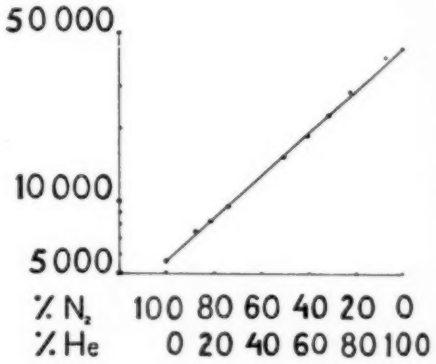

Diagram 3. The same relation as in Diagram 1 but for helium and nitrogen mixtures. Chamber length = 7.1 cm. Source = about 25 μC.

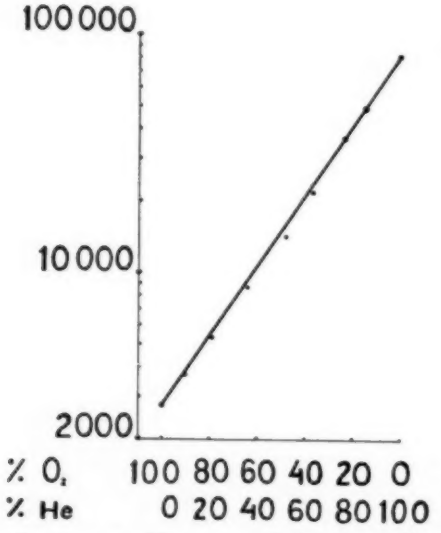

Diagram 2. The same relation as in Diagram 1 but with a chamber length of 9.3 cm, showing increased sensitivity of detection at the longer chamber length. Source = about 80 μC.

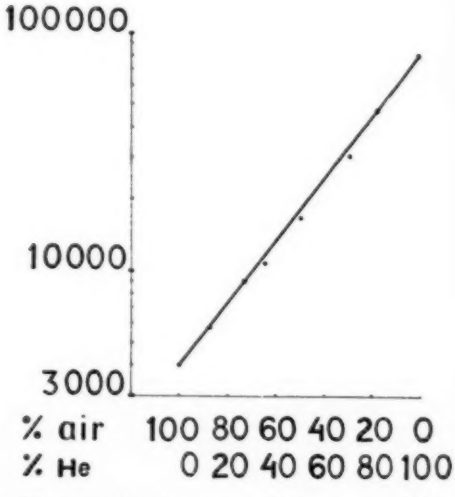

Diagram 4. The same relation as in Diagram 1 but for helium and air mixtures. Chamber length = 9.3 cm. Source = about 80 μC.

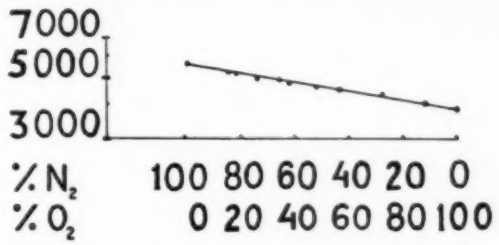

Diagram 5. The same relation as in Diagram 1 but for oxygen and nitrogen. Chamber length = 7.1 cm. Source = about 25 μC.

Discussion

After the convenient apparatus had been arranged, the analytical procedure with the present method was very simple. The composition of flowing gas could be analysed, as well as the composition of an enclosed gas volume, although we obtained certain data indicating that the rate of flow influenced the counting rate slightly. One advantage of the method presented is that the gas mixture analysed is in no way destroyed and that it can be used later for analysis with more conventional methods. The accuracy of the method may be increased if the number of counts is increased in order to reduce the statistical error and other precautions are undertaken to reduce systematical errors of various kinds, *e. g.* corrections introduced for the partial pressure of water vapour, barometric pressure, impurities of the gases from the bombs, temperature, decay of the S^{35} source (about 0.5 per cent per day), scattering, backscattering and nuclear interaction of beta rays, coincidence losses etc.

The minimum volume for analysis depends on the construction of the gas chamber. This can be made very narrow, thus reducing the gas volume considerably below the volume of about 10 cm^3 used for analysis in the present experiments. The gas column under analysis could also be made much shorter if some other radioisotope was chosen with less energetic beta rays, *e. g.* Ni^{63} (0.067 MeV, half-life 60 years) or H^3 (0.019 MeV, half-life 12 years).

One of the drawbacks of the method is that only binary gas mixtures may be analysed, and a gas mixture, containing three gases of unknown partial pressures, is beyond the limits of the beta ray transmission method. However, many problems of binary gas analysis arise, where this method will be applicable. We have, for example, started certain work on continuous gas analysis in connection with experimental and clinical spirometry.

SUMMARY

Transmission measurements of beta particles from S^{35} through gases have been performed and mixtures of He and O_2, He and air, He and N_2 and O_2 and N_2 analysed. An approximately linear relation between the partial pressures of the gas mixtures and the logarithm of the transmitted number of beta particles is reported.

ZUSAMMENFASSUNG

Transmissionsmessungen der Beta-Partikel von S^{35} durch Gase sind durchgeführt worden. Mischungen von He und O_2; He und Luft; He und N_2 und schliesslich O_2 und N_2 sind analysiert worden. Approximative lineare Relationen zwischen dem Partialdruck der Gasmischung und Logarithmus der transmittierten Anzahl der Beta-Partikel wurden gefunden.

RÉSUMÉ

Les auteurs ont fait des mesures de transmission de particules bêta émises par S^{35} à travers des gaz et ont analysé des mélanges de He et O_2, de He et d'air, de He et N_2 et de O_2 et N_2. Dans ces mélanges ils ont trouvé une relation approximativement linéaire entre les pressions partielles de ces mélanges gazeux et le logarithme du nombre de particules bêta transmises.

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EXPERIMENTAL APPROACHES TO THE BIOLOGIC ACTION OF ULTRAVIOLET RAYS

by

Gerard van der Schueren

Every living individual adapts itself to its environment by the bartering of material and photon energy. Hence, if we confine the notion of metabolism to the mere phases of absorption and excretion of chemical substances, the picture remains incomplete. Indeed, since the beginning of our century, the useful effect of ultraviolet rays on calcium fixation has been shown. About the same time, after the existence of shorter wave-lengths, artificially produced by discharges in vacuum under high voltages or liberated in nature by the splitting of heavy atoms, was discovered, their influence on living tissues came to light, often causing dramatic lesions in the first human investigators. The therapeutic action of these high energy radiations then soon became a first-line weapon against the dire neoplastic diseases.

Metabolism, in the broad sense, moreover may also reveal itself by electric currents of low intensity, as happens in the beating of the heart and the activity of the brain. Electrocardiograms even bring us definite information about the normal function and disturbances of these organs.

Hence, the energy borne by photons is not only artificially useful for therapeutic purposes, but interferes spontaneously, either in a normal or pathologic way, with the physiochemical phenomena in the cells. The concept of metabolism consequently receives a broader signification from the radiobiologic standpoint; to metabolism in the strict sense must be added not only the environmental wave-energy which interferes with the chemical composition of the living protoplasma, but also the electric energy given off.

Recent research on the biologic effect of the photon energy has stressed the production of peroxides. The gap between the physical effect of the

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rays and the other chemical phenomena in living beings seems to be becoming gradually filled.

Notwithstanding considerable experimental approaches, no definite agreement has been obtained on the problem of a possible biologic specificity of the different wave-lengths. The radiobiologic properties of a given gamma of the spectrum are usually interpreted more on a quantitative than a qualitative basis. The induction of peroxides *in vitro* and in the tissues is ascribed both to roentgen and to u.v. energy, although the absorption of gamma rays occurs on an atomic, and the absorption of the Finsen rays on a molecular, scale. Moreover, when the carcinogenic action of ultraviolet rays on the human skin has been considered, the hypothesis has been formulated that even neoplasms caused by radioactive substances or roentgen rays are induced by the breaking down of the short-wave-length energy of the latter in the tissues to the lower energy level of ultraviolet rays.

A few years ago, LACASSAGNE made a most interesting and complete survey of the physiochemical effects of electromagnetic waves. He suggested that the elective situations of squamous and undifferentiated carcinomas on the human face might be determined by the degree of absorption of ultraviolet light varying with the thickness of the skin: a basal cell epithelioma theoretically starting in the sub-epidermal cells should arise in regions with a thin epidermis, a spindle cell epithelioma, due to the proliferation of the germinative layer, in regions with a more developed epidermis. However, we found (15) no connection between the thickness of the epidermis and the situation of basal or spindle cell carcinomata.

Several research workers (12, 13 and others) have experimentally demonstrated the carcinogenic action of ultraviolet rays. A study in this field on albino mice was initiated in our laboratory many years ago (14). It has since been continued by a great number of co-workers (BONTE, POSCHET, VAN GANSEWINKEL, VERMEERSCH, VAN DER STAPPEN, CALLENS, et al.), and widely developed. A general survey of our positive results and an approach to the mechanism partly forms the subject of this communication.

The whole-body irradiation of several hundreds of albino mice was usually carried out, the animals being situated on the wires of a cylindric cage turning around a central axle. The animals belonged to a strain in which spontaneous skin cancer had never occurred. Each group averaged 25 mice and was irradiated every day over a period of from three to ten months.

Diagram 1 gives the percentage of tumours obtained in eight groups submitted to continuous and progressive irradiation. The results are calculated as absolute percentages based on the total number of animals

at the beginning of the experiment and as relative percentages based on the number of animals alive when the first tumour appeared. The difference between these two figures represents deaths during the weeks of irradiation preceding the first cancer.

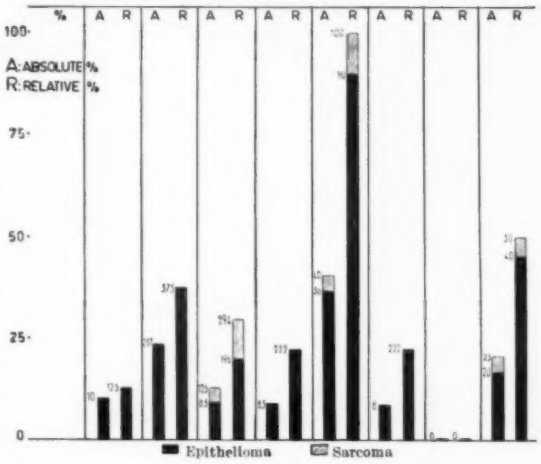

Diagram 1. Percentage of tumours in 8 groups submitted to progressive irradiation.

The total number of malignant tumours in relative percentage amounted to thirty-five. They arose on the hairless skin, notably of the ears, less seldom of the lower eyelid. Some research workers report having obtained the development of large tumours by u.v. irradiation. Although using much higher doses than commonly reported, we observed rather small tumours, often shown only by microscopic sections. The histologic type was usually an epithelioma, very seldom a sarcoma. Papillomata were, of course, observed in the first stage, but are not recorded in the results.

One group, irradiated every other day, exceptionally developed no neoplastic damage.

Cancer was produced only by frequently repeated, heavy doses of rays, containing a wave-length much shorter than the corresponding wave of a sun-ray beam dose. It took at least three months to induce a cancer. Metastases never occurred.

A few animals in every series, after several sessions, suddenly became paralysed, mostly in the hind-legs, with involvement of the anal and vesical sphincters. Moreover, after a few weeks of irradiation, a certain percentage of the albino mice died, even when all further exposure to ultraviolet radiation was stopped. The irradiation could usually be continued later without any more casualties. The histopathologic examination showed lesions of the parenchyma of the liver and kidney and discrete peribronchial densities in the lungs. Neither the haematologic pictures nor the determination of the oxidation metabolism in a great number of the irradiated mice explained the mechanism of death.

Owing to this difficulty, experiments were repeated in the frog in the hope that the pigment layer would afford a definite protection against

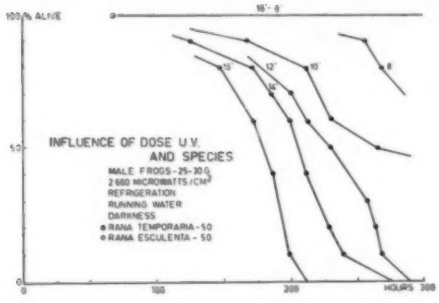

Diagram 2.

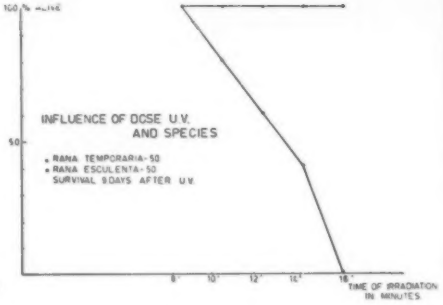

Diagram 3.

continuous irradiation with ultraviolet radiation. It was even hoped to induce skin cancer in this way, although the frog is very resistant to every variety of neoplastic disease. At the same time, a great number of other frogs were treated with benzopyrene, a strong carcinogenic agent for small rodents. The amphibians resisted the smearing of a large area of the skin for a long period and hardly developed any precancerous lesion (3).

The ultraviolet irradiation of the brown frog, species *Rana temporaria*, was carried out at a focus—skin distance of 50 cm to the hind-quarters of the fixed animal, over a period of 14 minutes. The spectrum of the ultraviolet lamp showed on a continuous back-ground a very energetic zone around the wave-length 3,000 Å (3,130 Å, 3,025 Å and 2,967 Å) and another around the wave-length 2,500 Å (2,650 Å and 2,537 Å).

The energy administered in these circumstances amounted to 2,660 micro-watts per square centimeter. After one single irradiation, all these brown frogs became ill and died a few days later. Since then, these experiments have been repeated in many hundreds of animals with practically always the same absolute result.

Repeating a routine experiment, we were extremely surprised that all the amphibians survived. A closer examination showed that this time the frogs were of a green type and belonged to the species *Rana esculenta*. This experiment was also repeated many times with the same result.

The conclusion may be drawn that the *Rana temporaria* and the *Rana esculenta* behave in a completely different manner to similar ultraviolet irradiation — all animals of the former group died, all those of the latter group survived.

There is even a mathematical relation between the dose of ultraviolet rays expressed by the duration of exposure and the rate of death of the brown frog. Diagram 2 shows the absolute survival of the *Rana esculenta* irradiated over a period of from 8 to 16 minutes. In the same circumstan-

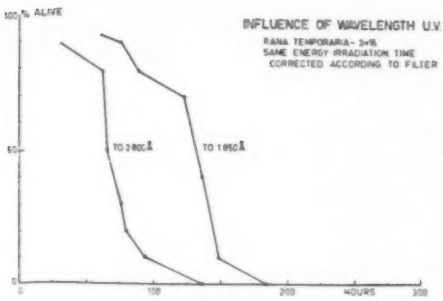

Diagram 4.

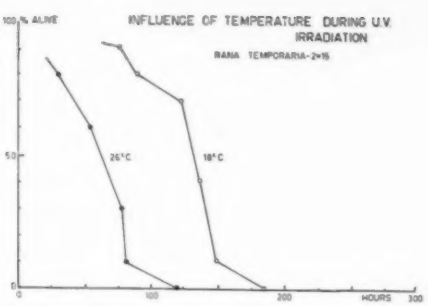

Diagram 5.

ces, all brown frogs, if exposed even for 12 minutes, die. If irradiated for 10 or 8 minutes, a more or less greater percentage survive. There is a striking progression in the rate of killing according to the dose.

On the ninth day a regular line (Diagram 3) joins the percentage of surviving animals in each group submitted to an increasing dose of ultraviolet light.

A first approach was made to examine which part of the ultraviolet spectrum appeared to be the most active. By the use of a filter, wavelengths shorter than 2,800 Å were cut off, and the loss of energy was compensated for either by an increase of exposure time or a shortening of the distance. A greater intensity of longer wave-length exerted a more abiotic effect (Diagram 4). It appeared as if the mechanism did not depend upon the wave-length, 2,537 Å, the action of which upon nucleoproteins is specific.

The temperature of the atmosphere around the animals is raised by the irradiation and readily reaches 26°C or more. This condition appeared to precipitate the lethal action of the ultraviolet rays as shown in Diagram 5. Cooling to room temperature by means of a ventilator did not prevent the lethal action, but delayed it. The infrared rays seem here to interfere with the ultraviolet rays, although the energy of the former is lessened by the thermic, the latter by the photo-electric effect.

Photorestoration has been proved in recent work on micro-organisms by several research workers (Monod, Torriani and Jolit, Kelner, Novick and Szilard, Latarjet and Caldas). Cultures of bacteria or streptomyces submitted to heavy doses of ultraviolet light recover if irradiated by visible light. In our experience the visible light was provided by a source delivering 300 Lux-units on the skin.

The experiments were performed in the most varied circumstances: with visible light administered before, during, or after u.v. irradiation.

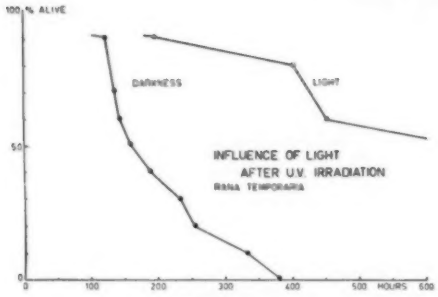

Diagram 6.

In the latter case, visible light was given at different periods, alternating with darkness, to test how long the lesions appeared reversible. These experiments are still going on. But we are already in a position to state that visible light administered before or during ultraviolet irradiation is devoid of any protective effect. On the contrary, if brown frogs are exposed for at least 24 hours during one of the three days following u.v. irradiation (Diagram 6), death is steadily delayed. In several groups the survival of a certain percentage of animals was noted and reached up to 50 per cent.

According to these results, namely the inhibitory power of visible light and the enhancing effect of temperature, the routine procedure in all our experiments consisted, except when otherwise stated, in keeping the animals refrigerated and in darkness.

The environmental factors influencing the radiologic damage as described all belong to the physical order: dose, wave-length, temperature and visible light. During the latent period following the absorption of radiant energy, chemical changes take place which lead to the lesion observable; these are mostly outside the scope of our investigation. As the skin absorbs nearly all the ultraviolet energy and, in the frog, plays an important rôle in the flux of sodium it seemed of interest to test the in- and outflow of this ion during the days following a lethal irradiation.

The dosage of sodium was measured both by the spectrophotometric method and the use of radioactive Sodium 24.

Firstly, a series of normal brown frogs, kept under the same conditions as the irradiated animals, were followed for their sodium exchange. The daily dosage of the sodium in the running water around the animals produces a surplus either of the inflow or outflow (Diagram 7). At the end of two weeks the flux approaches zero: the absorption and excretion reach equilibrium.

The irradiated animals, on the contrary, continually lose sodium except during the two last days before death (Diagram 8). During the ten days of survival, the total outflow amounts to 8.37 mg, the inflow to 2.57 mg. The sodium loss thus reaches 5.8 mg.

The skin of the irradiated brown frog becomes much more permeable for sodium as regards the outflow as is also proved by the following experiment.

Different groups of brown frogs, the cloaca of which had been tem-

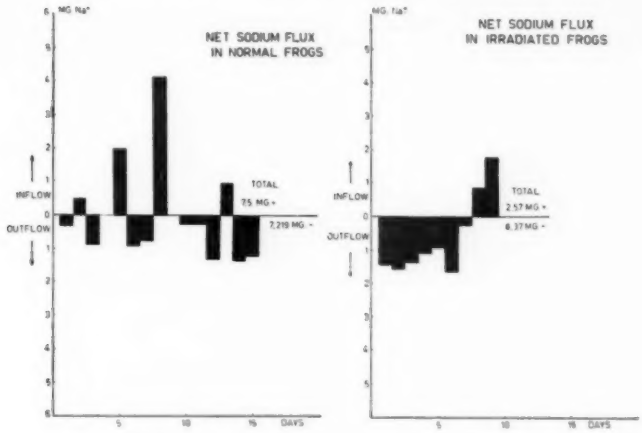

Diagram 7. Diagram 8.

porarily closed, received in the coelomic cavity 1 ml of a physiologic solution of sodium carbonate containing 1 to 10 microcuries of labelled sodium. Half of the animals had been irradiated, 24 days before, for 30 minutes with u.v. light, the second half being held as controls. The excretion of radiosodium was collected separately for every animal for five hours in 200 ml of tap water. One ml of the specimen was tested on the Geiger counter. The counts registered in each experimental animal were, after due correction, compared with the results obtained in a control. By comparison of the general average of counts it appeared that the outflow of radiosodium reached a value three-and-a-half times higher in the irradiated animals. The results of one such experiment recorded in Table 1 were confirmed several times.

Table 1

Transcutaneous outflow of radiosodium in counts/minute

Rana temporaria

Nr	After ultraviolet irradiation	Nr	Controls
1.	51.313	10	18.280
2.	56.000	11	13.485
3.	40.571	12	13.378
4.	23.096	13	7.251
5.	69.213	14	10.831
6.	55.842	15	19.327
7.	22.199	16	11.970
8.	52.101	17	9.904
9.	62.408	18	14.068
Average	48.082	average	13.166

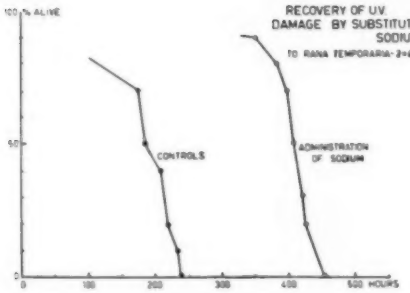

Diagram 9.

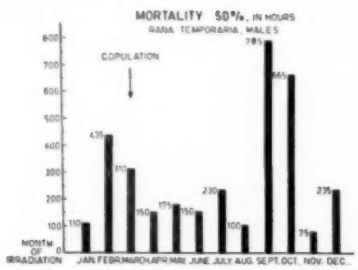
MORTALITY 50%, IN HOURS
RANA TEMPORARIA, MALES
COPULATION
MONTH OF IRRADIATION
JAN. FEBR. MARCH APR. MAY JUNE JULY AUG. SEPT. OCT. NOV. DEC.

Diagram 10.

Instead of injecting the sodium, the irradiated frogs may be kept in a bath containing radiosodium. As the amphibian lives in a continuous ionic skin exchange, a certain amount of radiosodium will be absorbed.

Eighteen hours later, each animal, the body surface of which has been carefully washed, is tested for sodium outflow over a period of five hours. The frogs exposed to ultraviolet rays again excrete more sodium than the controls, in fact approximately double the amount.

10 irradiated animals average	18.121 counts
20 controls average	10.864 counts

An increased outflow of sodium has also been demonstrated recently by KIRSCHNER by the application of tetraethylpyrophosphate to the interior surface, or of atropine, histamine or pilocarpine to the exterior surface, of isolated frog's skin. It is of interest to note that whereas the same results were obtained in *Rana esculenta* and *Rana temporaria* with anticholinesterase tetraethylpyrophosphate, only the former amphibian responded to atropine. This enzyme and these drugs influence acetylcholine metabolism which in its turn, as shown by ROTHENBERG and by HOLLAND, DUNN and GRIEG, modified ion movement in a variety of tissues; the presence of acetylcholinesterase was demonstrated (1) in the thrombocytes and erythrocytes of different animal species. If this is true for the frog, the destruction of the enzyme by ultraviolet light might be considered feasible.

The apparent disturbance of sodium metabolism by ultraviolet irradiation seemed to be an indication for testing whether the administration of this ion might delay or prevent death. As was to be expected, the mere restitution of the increased loss of sodium appeared to be without effect. Relatively high quantities of sodium, however, produced such effects that all the animals injected were alive when the irradiated controls had

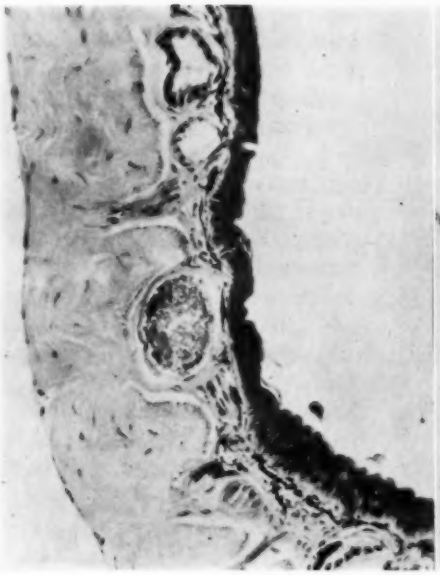

Fig. 1. Normal skin of brown frog.

Fig. 2. One hour after ultraviolet irradiation. The melanophores are contracted and the mucous glands in a phase of secretion. Marked edema.

died. But the result (Diagram 9) was only transitory and later those frogs protected with sodium, in their turn, succumbed.

It is evident that the disturbance of sodium flux must be connected in some manner with the histologic skin lesions induced by the radiant energy. Microscopic sections were prepared of the skin before, and in different stages after, irradiation.

The normal skin of the brown frog (Fig. 1) consists of an epidermis of the malpighian type with a nearly homogeneous and continuous layer of chromophores, especially melanophores, at the junction of the corium. The corium is composed of a superficial spongiosa and a deeper compacta layer. Granular and mucous glands are developed in the depth of the spongiosa. The mucous type is represented in far the greatest number: its cells are cylindric when in the secretion phase, and flattened when at rest. There is one granular gland in the section. Its lumen is filled with acidophil granules and its peripheral cells are of the stretched type. The spongiosa is further composed of loose connective tissue. At the junction of the spongiosa with the compacta, runs a lymphatic space, mostly well

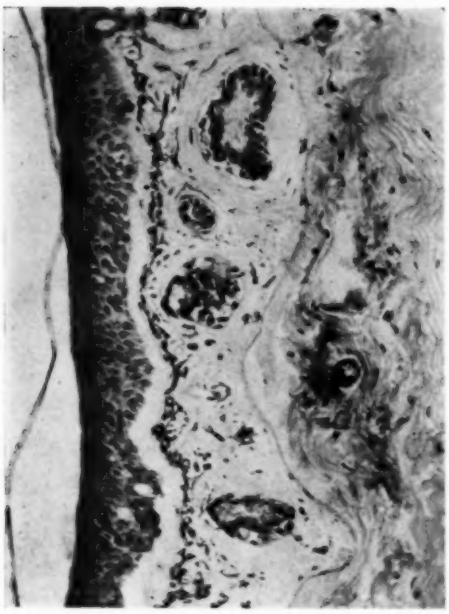

Fig. 3. Skin of green frog 48 hours after ultraviolet irradiation. A vesicle lifts the epidermis from the spongiosa. The melanophores show no tendency to contract.

limited by a continuous layer of basophil fibers. The compacta is built up of fibrous tissue.

One hour after the ultraviolet irradiation (Fig. 2) of a brown frog the melanophores become contracted and the mucous glands are in the phase of secretion. No granular glands are visible in the preparation. Marked edema is evident in the spongiosa which has doubled in thickness and compressed the lymphatic space. The latter has lost its basophil boundary on the side of the compacta. In a section obtained four days following the ultraviolet trauma, the corneal and, to some extent, the intermediate layer has become detached. The melanophores remain clumped. There is no eosinic colouration of the contents of the distended mucous glands. Marked edema continues to displace the spongiosa and partly detach it from the compacta. Eight days after irradiation, a few layers of the epidermis seem to have exhibited definite resistance. The melanophores do not spread out again as normally. The edema in the spongiosa is diminished, though the connective tissue, showing signs of necrosis, still extends broadly under the glands.

In the *Rana esculenta*, the histologic structure appears to be about the same, but the radiologic lesions occur somewhat differently. Forty-eight hours after the ultraviolet irradiation (Fig. 3) a vesicle lifts the epidermis from the spongiosa. The melanophores show no marked tendency to contract, but remain regularly at the surface of the spongiosa which is not swollen by edema. On the eighth day following the absorption of ultraviolet energy, the degenerated epidermis is cast off from the spongiosa which appears relatively free from damage.

Summarising the skin lesions induced by ultraviolet light, in the *Rana temporaria* these are characterised by damage to the spongiosa and in the *Rana esculenta* by lesions of the epidermis; in the former the

melanophores are contracted, in the latter they continue to be spread out and thus apparently to protect the spongiosa.

The increased outflow in the irradiated brown frog and a certain restoration effect of the sodium administered lose part of their importance if it is realized that the green frogs, though resistant to an ultraviolet dosage, lethal in the case of the brown frogs, behave somewhat in the same way as regards sodium metabolism. Indeed, their outflow as measured after an intracoelomic injection of Sodium 24 is increased and exceeds two-and-a-half times the outflow of the controls. This increase of sodium loss is not much lower in *Rana esculenta* than the values registered in *Rana temporaria*.

No definite results are at hand to justify comment regarding the storing of potassium in the different organs after irradiation. The material has already been prepared but the study of it has still to be made. We are able to state at any rate that irradiated brown frogs which received an injection in the coelomic cavity of a Ringer solution containing labelled-Potassium 42, excrete twice as much potassium as normal animals.

Endocrine factors certainly play a rôle on the sensitivity of the skin to ultraviolet rays. This problem is being investigated at the present time as part of our research work. Ever since the frog was used as the experimental subject in our laboratory, we have been struck by the fact that in certain periods of the year the animals appear resistant to ultraviolet rays and a low percentage even survive. For this reason, systematic irradiation of the same number of animals was performed every month. In Diagram 10, a dark column for every month of the year shows the number of hours it takes to kill 50 % of the brown frogs by ultraviolet rays. Two peaks are registered, one in February—March, corresponding to the copulation period, and another for which no explanation is yet available.

In the final part of this communication we present some experimental features which permit a closer comparison of the behaviour of the *Rana temporaria* and of the albino mouse to ultraviolet and roentgen rays.

Much has been said about the protective action of cyanide (2) against an otherwise lethal roentgen dosage. An explanation of this action is supposed to be a blocking of the oxidases and hence an inhibited production of peroxides by the radiation. We tried a great number of products in which the combination of CN appears in varying chemical compounds: sodium and potassium cyanide, potassium and ammonium ferrocyanide, potassium sulfocyanide and aceto- and benzonitril. Except when cyanide and especially sulfocyanide compound were used, all the results turned out negative. Sodium cyanide caused a slight inhibition when administered immediately before irradiation, but none after irradiation. The results with potassium sulfocyanide pointed in the same way, though

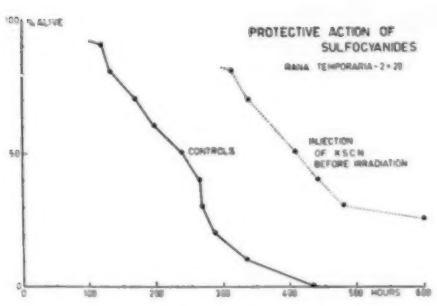

Diagram 11.

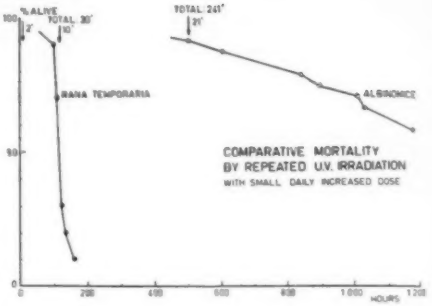

Diagram 12.

the protective effect of this chemical seemed the most active in this group. Following the administration of sulfocyanide (Diagram 11) in an average dose of 0.7 mg, the animals lived longer and in 30 % of the cases even survived completely.

As previously stated, a certain percentage of adult mice succumb but only after several sessions of relative high doses of ultraviolet rays, while frogs of the species *Rana temporaria* systematically die after one single, rather short irradiation. Moreover, the brown frog does not adapt itself to an increasing dosage as happens in man where long exposure to ultraviolet is tolerated if progressively applied. With an initial irradiation for two minutes, increased by the same amount at each session, all the *Ranae temporariae* die (Diagram 12) when a level of ten minutes is reached. On the other hand, the first mouse is lost after an exposure of only 21 minutes. The reason of this discrepancy in the sensibility to ultraviolet irradiation cannot be explained solely by the protection afforded by the hairy coat of the mouse; 24 albino mice the backs of which were completely shaved, were irradiated under the same conditions as the brown frog (Diagram 13) and all survived. And again, only 50 % new-born mice less than 24 hours old and consequently hairless, succumbed to ultraviolet irradiation; if irradiated when five days old, they all resisted.

As regards response to roentgen irradiation, the behaviour of the albino mouse and the *Rana temporaria* is strikingly the reverse. We could confirm the systematic lethality in mice of a roentgen dose of 850 r (200 kV, 0.5 mm Cu, F.S.D. 50 cm). Even a more than threefold dose (Diagram 14) remained completely harmless in the case of brown frogs. It may be of interest to note that a general roentgen bath, even with a dosage as high as 3,000 r, did not even double the excretion of radiosodium through the skin 24 hours after irradiation, and did not disturb it at all 26 days later. If the same amount of 3,000 r was ad-

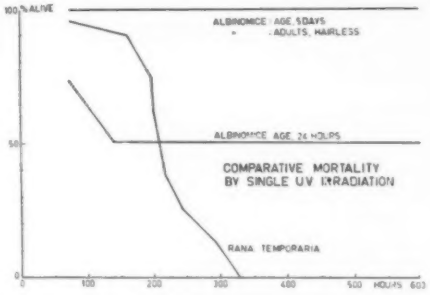

Diagram 13.

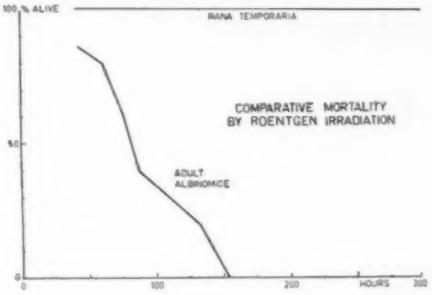

Diagram 14.

ministered in smaller fractions, the sodium balance remained quite unchanged immediately after the last session. It will be recalled that a small dose of ultraviolet energy nearly quadruples the excess of sodium outflow.

The extraordinary resistance of *Rana temporaria* to roentgen rays is also exerted against the exhibition of drugs employed succedaneously for roentgen treatment: urethane, nitrogen mustard and potassium arsenate. These chemicals may be administered to the frog also in extremely high doses without damage.

Conclusions

The carcinogenic property of ultraviolet light in mice is confirmed. Following the repeated application of large doses of ultraviolet radiation, paralysis and even death of a certain percentage of the animals occurred. At least 50 % of new-born and consequently hairless mice withstood thirty minutes' irradiation with ultraviolet rays.

One single irradiation (14 minutes at 50 centimeters) killed systematically all the frogs of species *Rana temporaria*, whereas all those of species *Rana esculenta* survived. There is even a mathematical relation between time of exposure and the death rate.

In the scale of the ultraviolet radiation, the longer waves exert a more abiotic effect. Raising the temperature around the animals during the exposure enhances the lethal effect of the radiation. On the other hand, visible light slows it down: this photorestoration even protected 50 % of the frogs from death.

The animals irradiated with ultraviolet radiation lose twice as much potassium, but 3.5 times as much sodium through the skin, as the controls. On the other hand, the administration of large amounts of sodium delayed death to a considerable extent.

The histopathologic picture reveals an early edema of the corium

and clumping together of the melanophores followed later by partial destruction of the epidermal layer. The lesions are mostly confined to the spongiosa in the *Rana temporaria*, whereas in the *Rana esculenta* it is the epidermis that is affected.

The resistance to ultraviolet is increased in two definite periods of the year, one of these being in February—March, the copulation period.

A relative chemical protection against this 'ultraviolet death' could be obtained especially by the use of potassium sulfocyanide.

The inversed reaction of albino mice and *Rana temporaria* to roentgen and ultraviolet rays is most striking. 850 r (200 kV, 50 cm, 0.5 mm Cu) kill all the albino mice, whereas 3,000 r appear harmless to the *Rana temporaria*. One irradiation of ultraviolet (14 minutes) is systematically lethal for *Rana temporaria*, whereas no adult albino mouse even if shaved, or five-day-old mice, succumb to a double dosage of the same rays.

SUMMARY

The results of experiments upon carcinogenesis by ultraviolet light in albino mice are reported. It is shown that one single, and not necessarily heavy, dose of ultraviolet radiation is lethal in a certain class of amphibians; the effect of protection is studied. The inversed reaction of albino mice and *Rana temporaria* to ultraviolet and roentgen rays is described and discussed.

ZUSAMMENFASSUNG

Die Ergebnisse der Experimente über die Karzinogenese bei Bestrahlung von Albinomäusen mit ultraviolettem Licht werden berichtet.

Es wird gezeigt, dass eine einmalige und nicht notwendigerweise hohe Dosis ultravioletter Strahlung für eine gewisse Klasse von Amphibien tödlich ist. Die Wirkung von Schutzanordnungen wird studiert. Die gegensätzliche Reaktion von Albinomäusen und *Rana temporaria* auf ultraviolette Strahlen und Röntgenstrahlen wird beschrieben und besprochen.

RÉSUMÉ

L'auteur rapporte les résultats d'expériences sur la carcinogénèse par la lumière ultra-violette chez des souris albinos. Il montre qu'une dose unique et pas nécessairement importante de rayons ultra-violets est léthale dans certaines classes d'amphibiens; il étudie l'effet de la protection. Il décrit et discute les réactions inverses aux rayons ultraviolets et aux rayons roentgen de la souris albinos et de *Rana temporaria*.

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BOOK REVIEW

THE CHEST. A HANDBOOK OF ROENTGEN DIAGNOSIS. By Leo G. Riegler. 2nd Edition. 380 pages, 338 illustrations. Year Book Publishers, Inc., Chicago 1954. $ 8.—.

In the preface to the first edition of his book the author wrote, "the atlas method of presentation seems peculiarly fitting for the elucidation of a field of roentgen diagnosis and it would seem to be especially suitable for the consideration of diseases of the thorax". These views on the way of publishing roentgen diagnostic matter seem rational, and one is readily willing to accept them. The atlas method compels the author to concentrate his text material so that it contains all essential matter but excludes everything that is irrelevant. Moreover, the term 'atlas' implies that the reproductions of roentgen films are of the highest standard. As regards the text, the book in question fulfills all that could be desired. It is seldom that one finds so much knowledge in an easily accessible form condensed in such a small and convenient volume. Despite its small size, it contains most of what a radiologist need know as regards techniques, normal roentgen anatomy, and pathologic conditions of the lungs, bronchi, mediastinum and pleura. Yet, if the text reaches our highest expectations, the same cannot be said about the reproductions of the roentgenograms. Anyone not previously acquainted with the typical appearance of these pathologic conditions must experience difficulties in obtaining information from the study of the illustrations. It is indeed surprising to find that reproductions in the American roentgenologic literature as a rule are often so unsatisfactory and but rarely compete with those ordinarily presented in European publications. This shortcoming is, however, to some degree offset by the excellent and clear captions which accompany the illustrations.

Under the heading 'Methods of examination', the author advocates a controversial principle: "Ideally, every patient presenting himself to a physician, regardless of his complaint, should have a fluoroscopic examination of the chest . . . It is likely that in the future this procedure will become an established routine." The reviewer's opinion is that if such a routine is to be valuable rather than harmful, one would necessarily expect the general physician to possess more knowledge of roentgen diagnostics than is generally the case. The author has also distinctly stated that a negative roentgen finding does not necessarily exclude the presence of pathologic conditions, even of a serious nature. A physician without knowledge of the difficulties of roentgen diagnostics is usually not sufficiently critical of his findings which, particularly if the examination reveals no abnormality, may easily engender in him, as well as his patient, a false sense of security.

Gunnar Jönsson.

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I. Åke Åkerlund: *Röntgenologische Studien über den Bulbus Duodeni.* 1921. (Out of print.)

II. Gösta Forssell: *On the Permanency of Radiological Healing in Malignant Tumours.* 1928. Price bound Sw. Kr. 10: —; unbound Sw. Kr. 8: —.

III. An account of the Second International Congress of Radiology, Stockholm, 1928. Price Sw. Kr. 15: —.

IV. Teaching and Training in Medical Radiology. Papers delivered at the Second International Congress of Radiology. 1930. Price Sw. Kr. 20: —.

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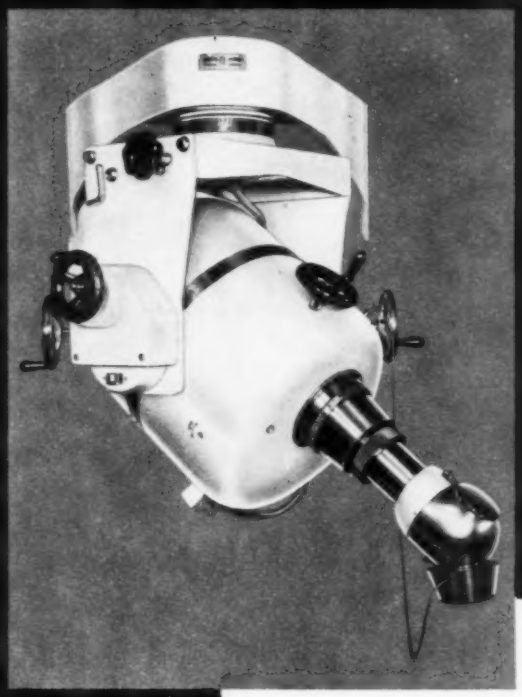

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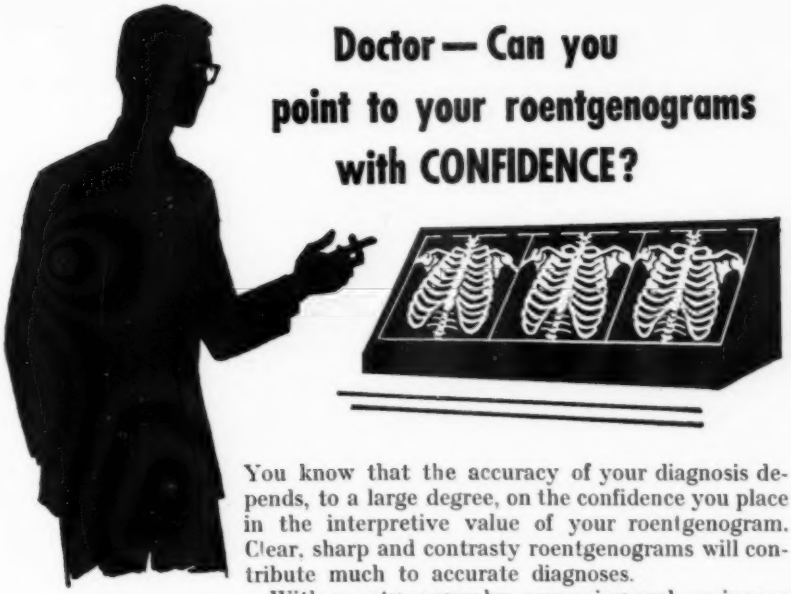

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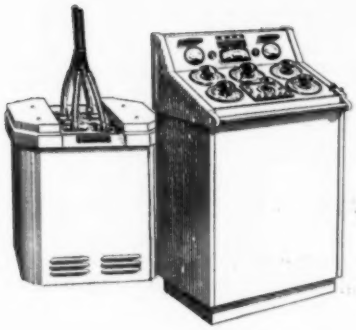

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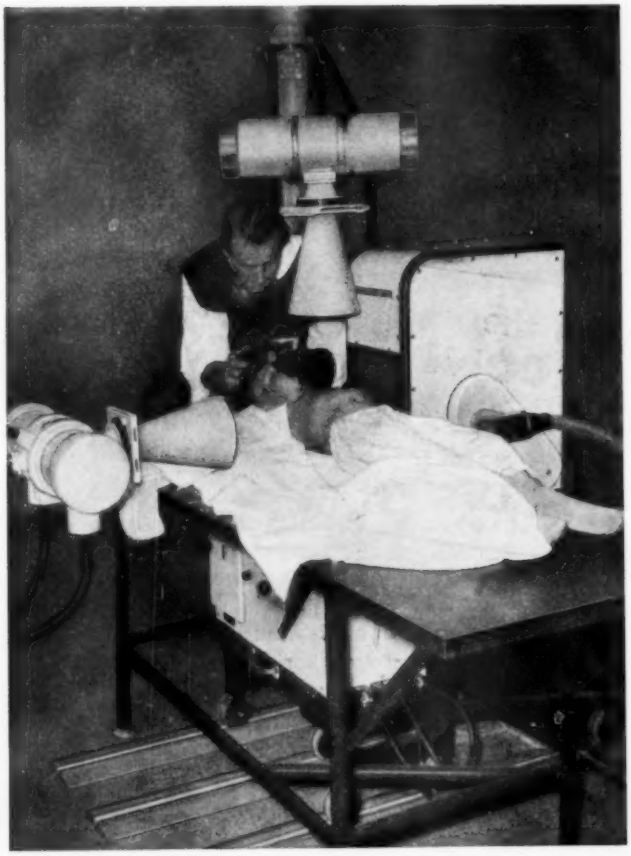

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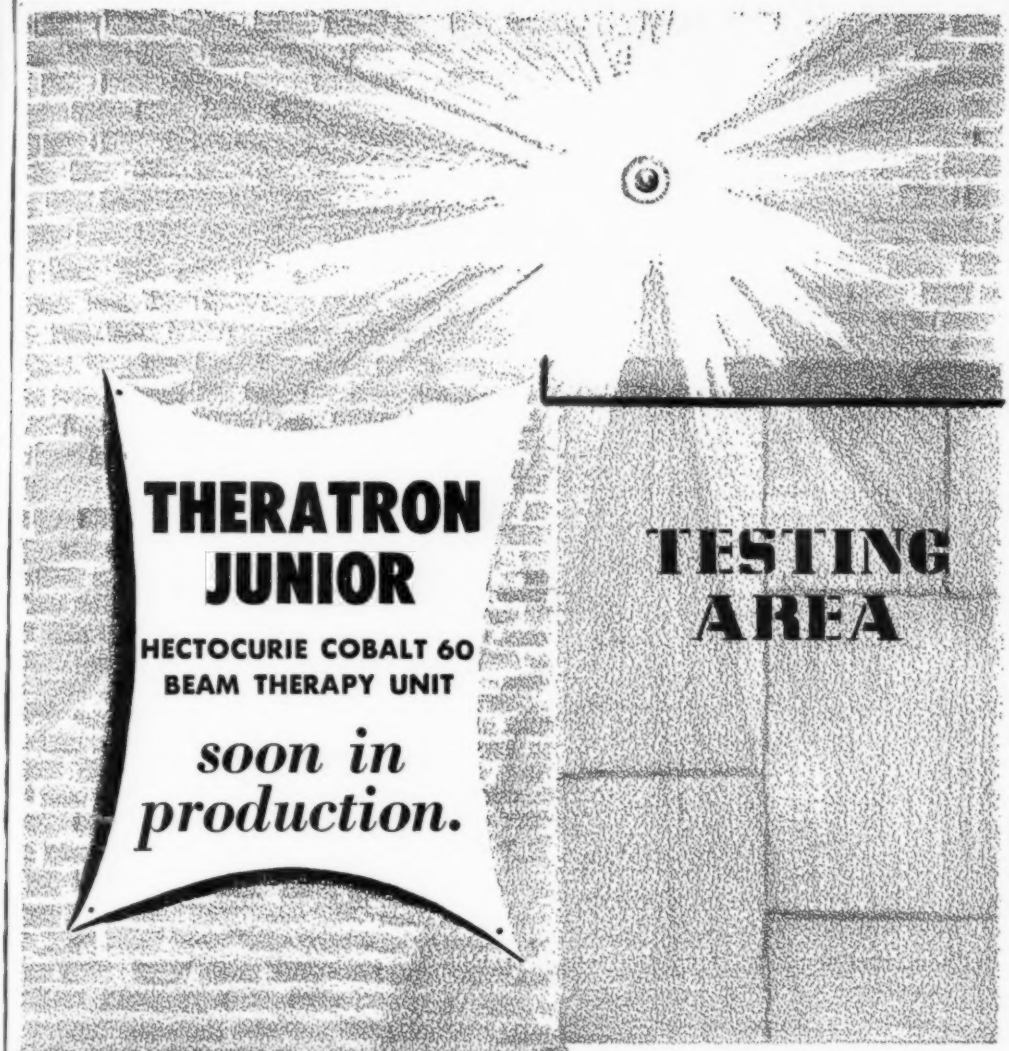

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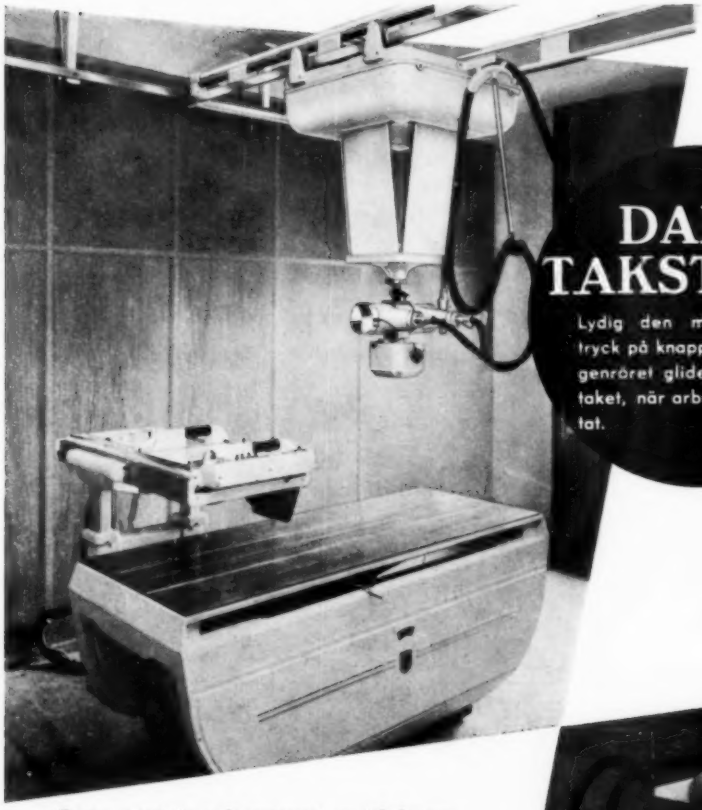

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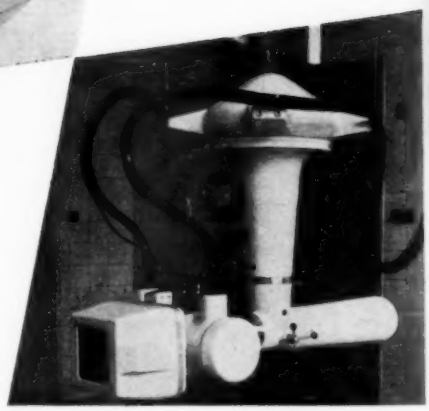

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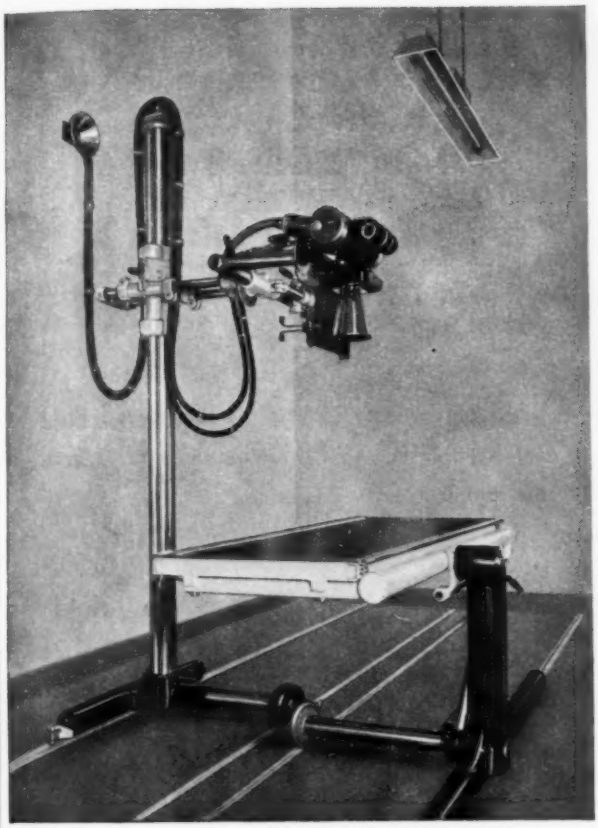

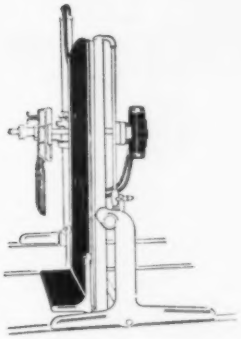

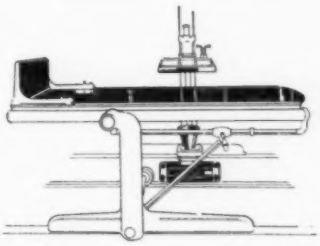

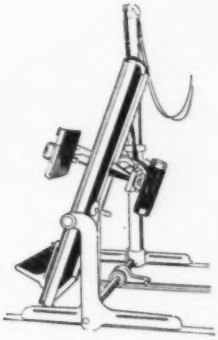

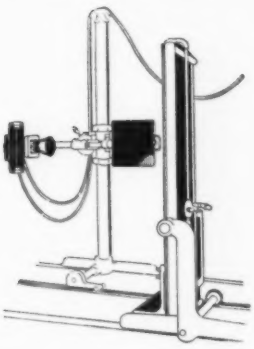

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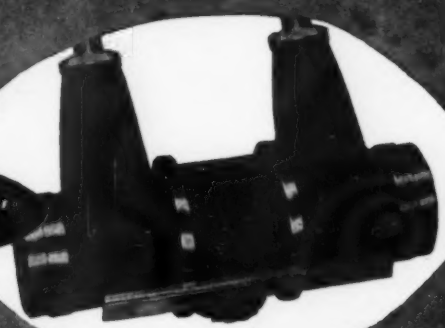

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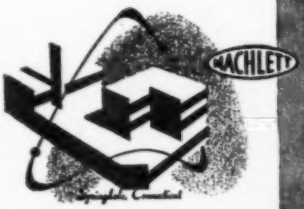


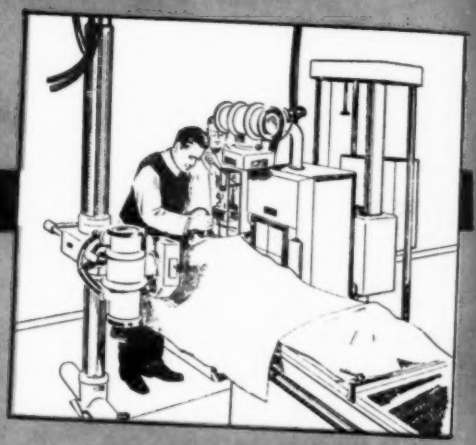
MACHLETT LABORATORIES, INC., SPRINGDALE, CONNECTICUT

THE ELEMA

BI-PLANE FILM CHANGER

for angiocardiography and angiography

Sidlund System



Model BST 641 for exposures simultaneously in two planes, film size 30×30 cm (12"×12") 50 radiographs in each plane.

Program selector for choosing picture frequency to correlate exposure conditions with the passage of contrast medium through the heart.

PICTURE FREQUENCY:
Type A1, 1 exp./10 sec. up to 8 exp./sec.
Type A3, 1 exp./10 sec. up to 12 exp./sec.

Complete equipment for heart investigation including high pressure syringe, catheters, electrocardiograph, blood pressure manometer, devices for easy processing of and drying roll-film, viewing box, and X-Ray apparatus with High Speed electronic contactor for primary switching.

The FILM CHANGER can be used with most types of X-Ray apparatus having sufficient output.

write for

further information on the Film Changer or address of our dealers which will be sent gladly on request.

ELEMA INDUSTRIVÄGEN 23 · STOCKHOLM-SOLNA · SWEDEN

A25-3501 DST 641